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NEWS 12 Jul 02 FOREGE no longer contains STANDARDS file segment  
NEWS 13 Jul 22 USAN to be reloaded July 28, 2002;  
saved answer sets no longer valid  
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NEWS 15 Jul 30 NETFIRST to be removed from STN  
NEWS 16 Aug 08 CANCERLIT reload  
NEWS 17 Aug 08 PHARMAMarketLetter(PHARMAML) - new on STN  
NEWS 18 Aug 08 NTIS has been reloaded and enhanced  
NEWS 19 Aug 19 Aquatic Toxicity Information Retrieval (AQUIRE)  
now available on STN  
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NEWS 22 Aug 26 Sequence searching in REGISTRY enhanced  
NEWS 23 Sep 03 JAPIO has been reloaded and enhanced  
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NEWS 25 Sep 16 Indexing added to some pre-1967 records in CA/CAPLUS  
NEWS 26 Sep 16 CA Section Thesaurus available in CAPLUS and CA  
NEWS 27 Oct 01 CASREACT Enriched with Reactions from 1907 to 1985  
NEWS 28 Oct 21 EVENTLINE has been reloaded  
NEWS 29 Oct 24 BEILSTEIN adds new search fields  
NEWS 30 Oct 24 Nutraceuticals International (NUTRACEUT) now available on STN  
NEWS 31 Oct 25 MEDLINE SDI run of October 8, 2002  
NEWS 32 Nov 18 DKILIT has been renamed APOLLIT  
NEWS 33 Nov 25 More calculated properties added to REGISTRY

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=> s immunogenic valency platform molecule?  
L1 0 IMMUNOGENIC VALENCY PLATFORM MOLECULE?

=> s immuno? (3a) platform  
L2 71 IMMUNO? (3A) PLATFORM

=> s l2 and (SLE or systemic lupus erythematosus)  
L3 1 L2 AND (SLE OR SYSTEMIC LUPUS ERYTHEMATOSUS)

=> s l2 and affinity  
L4 3 L2 AND AFFINITY

=> s l3 or l4  
L5 4 L3 OR L4

=> dup rem l5  
PROCESSING COMPLETED FOR L5  
L6 4 DUP REM L5 (0 DUPLICATES REMOVED)

=> d bib abs 1-  
YOU HAVE REQUESTED DATA FROM 4 ANSWERS - CONTINUE? Y/(N):y

L6 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2002 ACS  
AN 2001:434908 CAPLUS  
DN 135:41018  
TI Antibody \*\*\*affinity\*\*\*-based methods of treating lupus, screening methods, and compositions  
IN Linnik, Matthew D.; McNealy, Patricia A.  
PA La Jolla Pharmaceutical Company, USA  
SO PCT Int. Appl., 87 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
FAN.CNT 1  
PATENT NO. KIND DATE APPLICATION NO. DATE  
PI WO 2001041813 A2 20010614 WO 2000-US42307 20001128  
WO 2001041813 A3 20020103  
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
RW: GH, GM, KE, LS, MV, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG  
EP 1233791 A2 20020828 EP 2000-992252 20001128  
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR  
NO 2002002441 A 20020709 NO 2002-2441 20020523  
PRAI US 1999-167716P P 19991128  
WO 2000-US42307 W 20001128  
AB The invention provides methods identifying individuals suitable for treatment for lupus and methods of monitoring treatment, based on measuring antibody affinities, as well as of treating lupus based on measuring antibody affinities. The treatment entails administration of a conjugate comprising a non- \*\*\*immunogenic\*\*\* valency \*\*\*platform\*\*\* mol. and at least two double stranded DNA epitopes, such as DNA mols., which bind to anti-DNA antibodies from the patient.

L6 ANSWER 2 OF 4 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.  
AN 2001:314939 BIOSIS  
DN PREV200100314939  
TI Anti-dsDNA antibodies in \*\*\*SLE\*\*\*. Clinical evaluation of an ELISA and a new enzyme \*\*\*immunoassays\*\*\* on an automated \*\*\*platform\*\*\*, both using recombinant plasmid dsDNA.  
AU Hernando, M. (1); Gonzalez, C. (1); Sanchez, A.; Guevara, P. (1); Navajo, J. A. (1); Gonzalez-Buitrago, J. M. (1); Papisch, W.  
CS (1) Servicio de Bioquímica, Univesitario de Salamanca, Salamanca Spain  
SO Lupus, (2001) Vol. 10, No. Supplement 1, pp. S126, print.  
Meeting Info.: Sixth International Lupus Conference Barcelona, Spain March 24-28, 2001  
ISSN: 0961-2033.  
DT Conference  
LA English  
SL English

L6 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2002 ACS  
AN 2000:418584 CAPLUS  
DN 134:112558  
TI \*\*\*Immunoaffinity\*\*\*-based phosphorescent sensor \*\*\*platform\*\*\* for the detection of bacterial spores  
AU Scholl, Peter F.; Barger, C. Brent; Phillips, Terry E.; Wong, Tommy; Abubaker, Sala; Groopman, John D.; Strickland, Paul T.; Benson, Richard C.  
CS Applied Physics Lab., Johns Hopkins Univ., Laurel, MD, USA  
SO Proceedings of SPIE-The International Society for Optical Engineering (2000), 3913(In-Vitro Diagnostic Instrumentation), 204-214  
CODEN: PSISDG; ISSN: 0277-786X  
PB SPIE-The International Society for Optical Engineering  
DT Journal  
LA English

AB Consideration of emergency response plans to an attack with biol. weapons such as anthrax spores has spawned renewed interest in the development of inexpensive, rapid, and sensitive field portable sensors for use by non-specialists. The conceptual feasibility of such a device is demonstrated via the immunoaffinity capture of spores of the anthrax simulant B. globigii on a column followed by their washing, elution and phosphorescent detection. Spores are generically detected via the rapid extn. of dipicolinic acid (DPA) followed by its chelation with terbium to yield a phosphorescent complex. Chem., thermal and mech. methods of DPA extn. were evaluated. Simple extn. in HNO3 released up to 5% of the spore wt. as DPA within 60 s. Extn. in H2O liberated 7 % of the spore wt. as DPA. Sonication with glass beads in H2O for 45 s released up to 4 % of the spore wt. as DPA. It is estd. that implementation of these techniques will permit development of a device requiring 3-5 min per anal. with a limit of detection on the order of 500 ng spore/mL. This approach is not intended to replace more specific methods of anal. However, it is proposed for consideration as an inexpensive, simple and rapid means of spore detection by non-specialists in emergency situations.

RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2002 ACS

AN 1999:737068 CAPLUS

DN 131:348752

TI Miniature immuno-optical rapid analyte sensor platform

IN Anderson, Charles W.; Barger, C. Brent; Benson, Richard C.; Carlson, Micah A.; Fraser, Alan B.; Groopman, John D.; Ko, Harvey W.; Kohler, David R.; Phillips, Terry E.; Strickland, Paul T.

PA Johns Hopkins University, USA

SO PCT Int. Appl., 38 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9958975	A1	19991118	WO 1999-US10176	19990510
W: AU, BR, CA, CN, IN, JP, KR, MX, RU, SG, ZA				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6261848	B1	20010717	US 1998-74644	19980508
AU 9963084	A1	19991129	AU 1999-63084	19990510
EP 1075660	A1	20010214	EP 1999-922892	19990510
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002514763	T2	20020521	JP 2000-548727	19990510
US 2001053556	A1	20011220	US 2001-906243	20010718
PRAI US 1998-74644	A	19980508		
WO 1999-US10176	W	19990510		

AB A hand-held, self-contained, automatic, low power and rapid sensor platform for detecting and quantifying a plurality of analytes. A sample soln. potentially contg. an unknown amt. of an analyte is passed through an \*\*\*affinity\*\*\* column which contains antibodies to which the analyte binds thereby extg. the analyte. The \*\*\*affinity\*\*\* column is then rinsed to remove any other chems. that may fluoresce. The rinsed \*\*\*affinity\*\*\* column is then eluted with a known vol. of elution fluid causing the analyte to release from the antibody and dissolve in the fluid (eluant). The eluant is then placed in the quartz cuvette of a fluorometer. The analyte suspended in the eluant fluoresces at a wavelength which is different than that of the light source that excites it. The amt. of fluorescence is measured and the level of analyte detd. The rinsing and elution fluids, and/or the \*\*\*affinity\*\*\* column can be placed in a module for easy insertion and removal from the sensor when depleted or when the sensor is to be used against a different analyte.

RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his

(FILE 'HOME' ENTERED AT 14:14:50 ON 26 NOV 2002)

FILE 'BIOSIS, EMBASE, CAPLUS' ENTERED AT 14:30:51 ON 26 NOV 2002

L1 0 S IMMUNOGENIC VALENCY PLATFORM MOLECULE?  
L2 71 S IMMUNO? (3A) PLATFORM  
L3 1 S L2 AND (SLE OR SYSTEMIC LUPUS ERYTHEMATOSUS)  
L4 3 S L2 AND AFFINITY  
L5 4 S L3 OR L4  
L6 4 DUP REM L5 (0 DUPLICATES REMOVED)

=> s LJP 394

L7 56 LJP 394

=> dup rem l7

PROCESSING COMPLETED FOR L7

L8 40 DUP REM L7 (16 DUPLICATES REMOVED)

=> s l8 and affinity?

L9 4 L8 AND AFFINITY?

=> d bib abs 1-

YOU HAVE REQUESTED DATA FROM 4 ANSWERS - CONTINUE? Y/(N):y

L9 ANSWER 1 OF 4 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

AN 2001:445266 BIOSIS

DN PREV200100445266

TI Pre-treatment \*\*\*affinity\*\*\* for \*\*\*LJP\*\*\* \*\*\*394\*\*\* influences pharmacodynamic response in lupus patients.

AU McNeeley, P. A.; Iverson, G. M.; Furie, R. A.; Cash, J. M.; Cronin, M. E.; Katz, R. S.; Weisman, M. H.; Aranow, C.; Linnik, M. D. (1)

CS (1) La Jolla Pharmaceutical Co., 6455 Nancy Ridge Drive, San Diego, CA, 92121; linnik@ljpc.com USA

SO Lupus, (2001) Vol. 10, No. 8, pp. 526-532. print.

ISSN: 0961-2033.

DT Article

LA English

SL English

AB Five prospective clinical studies in lupus patients have shown that \*\*\*LJP\*\*\* \*\*\*394\*\*\* can reduce circulating anti-dsDNA antibody levels without causing generalized immunosuppression. The compound is currently being evaluated in a phase III clinical trial for the prevention of renal flares in patients with high- \*\*\*affinity\*\*\* antibodies to \*\*\*LJP\*\*\* \*\*\*394\*\*\* and a history of lupus nephritis. The current study analyzed the \*\*\*affinity\*\*\* of patient IgG for \*\*\*LJP\*\*\* \*\*\*394\*\*\* prior to and following 4 months of treatment with \*\*\*LJP\*\*\* \*\*\*394\*\*\* to determine if pretreatment \*\*\*affinity\*\*\* influenced pharmacodynamic response. Patient serum samples from a multicenter, double-blind, placebo-controlled trial were evaluated prior to and following 4 months of weekly, biweekly or monthly treatment with placebo (n=9) or weekly treatment with 10 mg \*\*\*LJP\*\*\* \*\*\*394\*\*\* (n=6) or 50 mg \*\*\*LJP\*\*\* \*\*\*394\*\*\* (n=4). After treatment there was a dose-dependent reduction in \*\*\*affinity\*\*\* in the 10 mg/week and 50 mg/week groups (P<0.05 and P<0.01, respectively), whereas the placebo group was unchanged. This study demonstrates that weekly treatment with \*\*\*LJP\*\*\* \*\*\*394\*\*\* produces a dose-dependent reduction in titer-weighted average \*\*\*affinity\*\*\*. These results suggest it may be possible to use an \*\*\*affinity\*\*\* assay to define prospectively patients that are most likely to exhibit the desired pharmacodynamic response to \*\*\*LJP\*\*\* \*\*\*394\*\*\*.

L9 ANSWER 2 OF 4 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

AN 2001:319917 BIOSIS

DN PREV200100319917

TI SLE trial shows fewer renal flares in \*\*\*LJP\*\*\* \*\*\*394\*\*\* -treated patients with high- \*\*\*affinity\*\*\* antibodies to \*\*\*LJP\*\*\* \*\*\*394\*\*\* : 90-05 Trial results.

AU Alarcon-Segovia, D. (1); Tumlin, J. (1); Furie, R. (1); McKay, J. (1); Cardiel, M. (1); Linnik, M. (1); Hepburn, B. (1)

CS (1) La Jolla Pharmaceutical Co., San Diego, CA USA

SO Lupus, (2001) Vol. 10, No. Supplement 1, pp. S94. print.

Meeting Info.: Sixth International Lupus Conference Barcelona, Spain March 24-28, 2001

ISSN: 0961-2033.

DT Conference

LA English

SL English

L9 ANSWER 3 OF 4 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

AN 2001:319912 BIOSIS

DN PREV200100319912

TI \*\*\*Affinity\*\*\* of antibodies for \*\*\*LJP\*\*\* \*\*\*394\*\*\* influences pharmacodynamic response to \*\*\*LJP\*\*\* \*\*\*394\*\*\* in SLE patients.

AU Linnik, M. D. (1); McNeeley, P. A. (1); Iverson, G. M. (1)

CS (1) La Jolla Pharmaceutical Co., San Diego, CA USA

SO Lupus, (2001) Vol. 10, No. Supplement 1, pp. S52. print.

Meeting Info.: Sixth International Lupus Conference Barcelona, Spain March 24-28, 2001

ISSN: 0961-2033.

DT Conference

LA English

SL English

L9 ANSWER 4 OF 4 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

AN 2001009805 EMBASE

TI Clinical and pharmacological experience with \*\*\*LJP\*\*\* - \*\*\*394\*\*\*.

AU Wallace D.J.

CS D.J. Wallace, Clinical Professor of Medicine, Cedars-Sinai Univ. of California LA, 8737 Beverly Blvd, Los Angeles, CA 90048, United States. dwallace@ucla.edu

SO Expert Opinion on Investigational Drugs, (2001) 10/1 (111-117).

Refs: 12

ISSN: 1354-3784 CODEN: EOIDER

CY United Kingdom

DT Journal: Article

FS 026 Immunology, Serology and Transplantation

030 Pharmacology

037 Drug Literature Index

038 Adverse Reactions Titles

LA English

SL English

AB \*\*\*LJP\*\*\* - \*\*\*394\*\*\* is a synthetic biological with immunomodulatory functions. Composed of four double-stranded oligodeoxynucleotides attached to a central branched platform, the drug acts as an anti-anti-ds-DNA B-cell toleragen by rendering specific B-lymphocytes unresponsive to immunogen so they do not produce autoantibodies. Extensive animal studies and Phase II clinical trials suggested that the effects of \*\*\*LJP\*\*\* - \*\*\*394\*\*\* are effective and safe when used as a weekly dose of 100 mg intravenously. Analysis of a multicentre, international Phase II/III clinical trial showed that patients with lupus nephritis and high \*\*\*affinity\*\*\* IgG antibodies to \*\*\*LJP\*\*\* - \*\*\*394\*\*\* have clinical benefits. This includes increased time to renal flares, reduced number of renal flares, time to institution of high-dose corticosteroids and/or cyclophosphamide and lower anti-ds-DNA levels. A definitive trial is in progress. \*\*\*LJP\*\*\* - \*\*\*394\*\*\* appears to be free of serious adverse reactions. Though promising, the role of \*\*\*LJP\*\*\* - \*\*\*394\*\*\* in patients with active, organ-threatening lupus is still not known.

=> s non immunogenic valency platform

L10 1 NON IMMUNOGENIC VALENCY PLATFORM

=> d bib abs

L10 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2002 ACS

AN 2001:434908 CAPLUS

DN 135:41018

TI Antibody affinity-based methods of treating lupus, screening methods, and compositions

IN Linnik, Matthew D.; McNealy, Patricia A.

PA La Jolla Pharmaceutical Company, USA

SO PCT Int. Appl., 87 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001041813	A2	20010614	WO 2000-US42307	20001128
WO 2001041813	A3	20020103		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,

CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1233791 A2 20020828 EP 2000-992252 20001128

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

NO 200202441 A 20020709 NO 2002-2441 20020523

PRAI US 1999-167716P P 19991128

WO 2000-US42307 W 20001128

AB The invention provides methods identifying individuals suitable for treatment for lupus and methods of monitoring treatment, based on measuring antibody affinities, as well as of treating lupus based on measuring antibody affinities. The treatment entails administration of a conjugate comprising a \*\*\*non\*\*\* - \*\*\*immunogenic\*\*\* \*\*\*valency\*\*\* \*\*\*platform\*\*\* mol. and at least two double stranded DNA epitopes, such as DNA mols., which bind to anti-DNA antibodies from the patient.

=> s anti-dsDNA antibod?

L11 1064 ANTI-DSDNA ANTIBOD?

=> s I11 and SLE

L12 581 L11 AND SLE

=> s I12 and affinit?

L13 54 L12 AND AFFINIT?

=> dup rem I13

PROCESSING COMPLETED FOR L13

L14 25 DUP REM L13 (28 DUPLICATES REMOVED)

=> d bib abs 1-

YOU HAVE REQUESTED DATA FROM 25 ANSWERS - CONTINUE? Y(N):y

L14 ANSWER 1 OF 25 CAPLUS COPYRIGHT 2002 ACS

AN 2002:839871 CAPLUS

TI Efficacy of IVIG \*\*\*affinity\*\*\* -purified anti-double-stranded DNA anti-idiotypic antibodies in the treatment of an experimental murine model of systemic lupus erythematosus

AU Shoenfeld, Yehuda; Rauova, Lubica; Gilburd, Boris; Kvapil, Filip;

Goldberg, Iris; Kopolovic, Jozef; Rovinsky, Jozef; Blank, Miri

CS Center for Autoimmune Diseases, Department of Internal Medicine B, Andorra

SO International Immunology (2002), 14(11), 1303-1311

CODEN: INIMEN; ISSN: 0953-8178

PB Oxford University Press

DT Journal

LA English

AB Since the idiotypic network is an important mechanism for controlling the immune repertoire, we tested anti-idiotypic modulation employing concd. specific natural polyclonal anti-double-stranded (ds) DNA anti-idiotypic antibodies obtained from a com. IVIG in the treatment of exptl. systemic lupus erythematosus ( \*\*\*SLE\*\*\* ). Specific natural polyclonal anti-dsDNA anti-idiotypic antibodies (IVIG-ID) were \*\*\*affinity\*\*\* purified from IVIG on an anti-dsDNA-Sepharose column constructed from anti-dsDNA idiotype (ID) \*\*\*affinity\*\*\* purified from 55 patients with active \*\*\*SLE\*\*\*. NZBW F1 mice were treated i.v. with 3 weekly injections of IVIG-ID (2 mg/kg/injection) or regular IVIG (400 mg/kg/injection) both before (age 8 wk) and after developing \*\*\*anti\*\*\* - \*\*\*dsDNA\*\*\* \*\*\*antibodies\*\*\* at the age of 21-22 wk. The IVIG-ID-treated mice showed a decline in the titer of \*\*\*anti\*\*\* - \*\*\*dsDNA\*\*\* \*\*\*antibodies\*\*\* during the treatment, reaching max. suppression 1 wk after the last injection. A significant difference in the proteinuria level in the IVIG-ID-treated group compared to the control group was obsd. Immunohistol. showed different patterns of IgG deposition, with mesangial and capillary wall deposits in controls and in the IVIG-treated group, but only mesangial deposits in the IVIG-ID-treated group. The survival time of the IVIG-ID-treated group was longer than the IVIG-treated group. Treatment with concd. specific anti-dsDNA anti-ID prep. from com. IVIG is more effective in suppressing the humoral reaction and clin. signs of \*\*\*SLE\*\*\* than native IVIG. These results point to the considerable regulatory role of anti-ID in the mechanism of action of IVIG in \*\*\*SLE\*\*\*.

L14 ANSWER 2 OF 25 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE

1

AN 2002:439104 BIOSIS

DN PREV200200439104

TI Production and characterization of human monoclonal anti-idiotypic antibodies to \*\*\*anti\*\*\* - \*\*\*dsDNA\*\*\* \*\*\*antibodies\*\*\*

AU Zhang, W.; Frank, M. B.; Reichlin, M. (1)

CS (1) Oklahoma Medical Research Foundation, Oklahoma City, OK, 73104;

Morris-Reichlin@omrf.ouhsc.edu USA

SO Lupus, (2002) Vol. 11, No. 6, pp. 362-369. print.

ISSN: 0961-2033.

DT Article

LA English

AB Anti-dsDNA autoantibodies are the hallmark of systemic lupus erythematosus ( \*\*\*SLE\*\*\* ) and frequently correlate with disease activity. In this study we report the isolation and characterization of human anti-Id monoclonal antibody fragments as single-chain Fv fragments (scFv) against \*\*\*anti\*\*\* - \*\*\*dsDNA\*\*\* \*\*\*antibody\*\*\*. The anti-Id monoclonal antibodies, specific for \*\*\*anti\*\*\* - \*\*\*dsDNA\*\*\* \*\*\*antibodies\*\*\*, have been cloned from phage display antibody scFv libraries derived from a patient with \*\*\*SLE\*\*\*. The V gene repertoires were derived from the RNA obtained from the B cells of an \*\*\*SLE\*\*\* patient with anti-Ro/SSA and anti-La/SSB antibodies. \*\*\*Affinity\*\*\* -purified \*\*\*anti\*\*\* - \*\*\*dsDNA\*\*\* \*\*\*antibodies\*\*\* were used for selection of bacterial clones producing specific scFv antibody fragments against \*\*\*anti\*\*\* - \*\*\*dsDNA\*\*\* \*\*\*antibodies\*\*\* and little reactivity with normal IgG and other IgG antibodies by ELISA. The anti-Id antibody recognizes a public idiotype that is broadly cross-reactive with polyclonal and monoclonal \*\*\*anti\*\*\* - \*\*\*dsDNA\*\*\* \*\*\*antibodies\*\*\*. This binding was largely inhibited by dsDNA antigen. The anti-Id antibody inhibited anti-dsDNA binding to dsDNA antigen in immunoassays and in the Crithidia luciliae assay. The anti-Id scFv antibody fragments derived from human genes could modulate the pathogenicity of anti-dsDNA autoantibodies and may have therapeutic implications in \*\*\*SLE\*\*\*. They may also be used as probes in studies of the structure of the idiotype.

L14 ANSWER 3 OF 25 EMBASE COPYRIGHT 2002 ELSEVIER SCI.

B.V.DUPLICATE 2

AN 2002362399 EMBASE

TI Evaluation of a new automated enzyme fluoroimmunoassay using recombinant plasmid dsDNA for the detection of \*\*\*anti\*\*\* - \*\*\*dsDNA\*\*\*

\*\*\*antibodies\*\*\* in \*\*\*SLE\*\*\*.

AU Villalta D.; Bizzaro N.; Corazza D.; Tozzoli R.; Tonutti E.

CS Dr. N. Bizzaro, Laboratorio di Patologia, Clinica Ospedale Civile, 30027

S. Dona di Piave (VE), Italy. nbizzaro@dacos.it

SO Journal of Clinical Laboratory Analysis, (2002) 16/5 (227-232).

Refs: 22

ISSN: 0887-8013 CODEN: JCANEM

CY United States

DT Journal; Article

FS 022 Human Genetics

026 Immunology, Serology and Transplantation

029 Clinical Biochemistry

LA English

SL English

AB ELISA methods to detect anti-double-stranded DNA ( \*\*\*anti\*\*\* -

\*\*\*dsDNA\*\*\* ) \*\*\*antibodies\*\*\* are highly sensitive, but are less specific for the diagnosis of \*\*\*SLE\*\*\* than the immunofluorescence test on Crithidia luciliae (CLIFT) and the Farr assay because they also detect low-avidity antibodies. This study evaluated the specificity,

sensitivity, positive predictive value (PPV), and negative predictive value (NPV) of a new automated fluoroimmunoassay (EliA dsDNA; Pharmacia, Freiburg, Germany). We compared the results with those obtained using a commercial CLIFT and an in-house anti-dsDNA IgG ELISA method, and verified its putative ability to detect only high-avidity \*\*\*anti\*\*\* - \*\*\*dsDNA\*\*\* \*\*\*antibodies\*\*\*. Sera from 100 \*\*\*SLE\*\*\* patients

and 120 controls were studied. The control group included 20 healthy donors, 70 patients with other rheumatic diseases (32 systemic sclerosis (SSc), 18 primary Sjogren syndrome (pSS), 20 rheumatoid arthritis (RA)), and 30 patients with various infectious diseases (ID). Anti-dsDNA avidity was estimated using an ELISA method based upon the law of mass action, and a simplified Scatchard plot analysis for data elaboration; the apparent \*\*\*affinity\*\*\* constant (Kaa) was calculated and expressed as arbitrary units (L/U). Sensitivity, specificity, PPV, and NPV for \*\*\*SLE\*\*\* were 64%, 95.8%, 93.8% and 72.7%, respectively, for the ELIA anti-dsDNA assay; 55%, 99.2%, 98.5%, and 68.8%, respectively, for the CLIFT; and 64%, 93.3%, 90.6%, and 72.3%, respectively, for the in-house ELISA. Although ELIA anti-dsDNA was positive mainly in \*\*\*SLE\*\*\* patients with high- (Kaa>80 L/U) and intermediate- (Kaa 30-80 L/U) avidity antibodies (45.3% and 49.9%, respectively), it was also positive in five (7.8%) \*\*\*SLE\*\*\* patients with low-avidity \*\*\*anti\*\*\* - \*\*\*dsDNA\*\*\*  
 \*\*\*antibodies\*\*\*, and five controls (three SSc, one pSS, and one ID) (mean Kaa = 16.4 +/- 9.04 L/U). In conclusion, ELIA anti-dsDNA assay showed a higher sensitivity than the CLIFT, and a good specificity and PPV for \*\*\*SLE\*\*\*. Its putative ability to detect only high-avidity \*\*\*anti\*\*\* - \*\*\*dsDNA\*\*\* \*\*\*antibodies\*\*\* remains questionable.  
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L14 ANSWER 4 OF 25 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

AN 2002:291263 BIOSIS

DN PREV200200291263

TI The effects of \*\*\*affinity\*\*\* -purified anti-DNA antibodies from patients with systemic lupus erythematosus on the fluorescent antinuclear antibody assay using HEP-2 cells.

AU Suzuki, Kimihiro (1); Kawamura, Masahide; Mineo, Midori; Shinohara, Tadashi; Kataharada, Koji; Okada, Makoto; Takada, Kunio; Miyawaki, Shoji; Ohsuzu, Fumitaka

CS (1) Internal Medicine I, National Defense Medical College, Namiki 3-2, Tokorozawa, Saitama, 359-8513: kogen@me.ndmc.ac.jp Japan

SO Clinical Chemistry and Laboratory Medicine, (January, 2002) Vol. 40, No. 1, pp. 46-51. print.

ISSN: 1434-6621.

DT Article

LA English

AB The aim of this study was to clarify the effects of \*\*\*anti\*\*\* -

\*\*\*dsDNA\*\*\* \*\*\*antibodies\*\*\* on the titer and the nuclear staining pattern(s) in a fluorescent antinuclear antibody (FANA) assay using HEP-2 cells. Anti-dsDNA derived from 14 patients with systemic lupus erythematosus ( \*\*\*SLE\*\*\* ) was individually \*\*\*affinity\*\*\* -purified. The anti-dsDNA titer of the purified anti-dsDNA solution was measured by radioimmunoassay (RIA) or by enzyme-linked immunosorbent assay

(ELISA). In the FANA assay, the anti-dsDNA solution was diluted in a stepwise manner and its titer was expressed by the endpoint dilution. The nuclear staining pattern in the anti-dsDNA solution was examined at the 1:5 and 1:20 dilutions and at the endpoint dilution. The anti-dsDNA titers of the \*\*\*affinity\*\*\* -purified anti-dsDNA solution were high enough (13 to 126 IU/ml) to be measured by RIA. However, the antinuclear antibody (ANA) titers of this solution were relatively low: 1:20 to 1:320. In the study of nuclear staining the peripheral pattern was observed in nine of the 14 cases at a 1:5 dilution. However, at the endpoint dilution, all cases exhibited the homogeneous pattern. These findings indicate that in the FANA assay using HEP-2 cells, 1) although serum samples show high anti-dsDNA titers by RIA or by ELISA, the antibodies' direct contribution to ANA titers is limited, and 2) when samples reveal a homogeneous staining pattern at the endpoint dilution, this suggests the presence of anti-dsDNA.

L14 ANSWER 5 OF 25 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE

3

AN 2001:357551 BIOSIS

DN PREV200100357551

TI Crossreactivity of human \*\*\*anti\*\*\* - \*\*\*dsDNA\*\*\* \*\*\*antibodies\*\*\* to phosphorylcholine: Clues to their origin.

AU Shama, Arti; Isenberg, David A.; Diamond, Betty (1)

CS (1) Department of Microbiology and Immunology and Medicine, Albert Einstein College of Medicine, 1300 Morris Park Avenue, Bronx, NY, 10461: diamond@aecom.yu.edu USA

SO Journal of Autoimmunity, (June, 2001) Vol. 16, No. 4, pp. 479-484. print. ISSN: 0896-8411.

DT Article

LA English

SL English

AB The presence of anti-double stranded DNA (dsDNA) antibodies is a serological diagnostic feature of systemic lupus erythematosus ( \*\*\*SLE\*\*\* ), an autoimmune rheumatic disorder. Studies by several investigators have suggested that a response to a microbial antigen can lead to the induction of \*\*\*SLE\*\*\* -like autoimmunity, in both humans and mice, since \*\*\*anti\*\*\* - \*\*\*dsDNA\*\*\* \*\*\*antibodies\*\*\* have been shown to crossreact with foreign antigens. In particular, anti-DNA antibodies have been shown to crossreact with phosphorylcholine (PC), a dominant epitope on pneumococcal cell wall polysaccharide. We have investigated the binding characteristics of human polyclonal anti-DNA antibodies from the sera of \*\*\*SLE\*\*\* patients. In this study we show that the DNA binding of polyclonal serum derived antibodies can be partially inhibited by phosphorylcholine (PC). The binding of \*\*\*affinity\*\*\* -purified anti-DNA antibodies from the sera of patients

with \*\*\*SLE\*\*\* was also found to be inhibited by PC. We further demonstrated that the serum IgG1 (T dependent) anti-DNA response was more likely to crossreact with PC than the IgG2 (T independent) response to DNA. The studies suggest there may be a T dependent and T independent response to DNA with the T dependent response displaying more crossreactivity with microbial antigen.

L14 ANSWER 6 OF 25 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE

4

AN 2001:115373 BIOSIS

DN PREV200100115373

TI Peptide mimicking antigenic and immunogenic epitope of double-stranded DNA in systemic lupus erythematosus.

AU Sun, Yongjiang; Fong, Kok-Yong; Chung, Maxey C. M.; Yao, Zhi-Jian (1)

CS (1) National Center for Human Genome Research, BDA, No. 3-707 North Yongchang Road, Beijing, 100176 China

SO International Immunology, (February, 2001) Vol. 13, No. 2, pp. 223-232. print.

ISSN: 0953-8178.

DT Article

LA English

SL English

AB Autoantibodies to double-stranded (ds) DNA are an important diagnostic marker and pathogenic factor for systemic lupus erythematosus ( \*\*\*SLE\*\*\* ). Identifying dsDNA mimotopes is a way to discover diagnostic and therapeutic candidates for \*\*\*SLE\*\*\*. 'Mono-specific' \*\*\*SLE\*\*\* \*\*\*anti\*\*\* - \*\*\*dsDNA\*\*\* \*\*\*antibodies\*\*\* were obtained by \*\*\*affinity\*\*\* purification using dsDNA-coupled Sepharose column. Using the \*\*\*anti\*\*\* - \*\*\*dsDNA\*\*\* \*\*\*antibodies\*\*\* to screen a phage peptide library, we were able to identify a mimotope that has a motif peptide sequence of RLTSRLRYNP. This chemically synthesized peptide could be recognized by 88% (37 out of 42) of \*\*\*anti\*\*\* - \*\*\*dsDNA\*\*\* \*\*\*antibody\*\*\* -positive \*\*\*SLE\*\*\* sera with a cut-off point at mean + 3 SD of the negative control sera at OD492. The reaction of the peptide with \*\*\*SLE\*\*\* sera in ELISA was highly correlated with that of dsDNA (r = 0.809, P < 0.0001). Of particular interest, not only dsDNA but also single-stranded (ss) DNA and native RNA could inhibit the binding of the peptide with \*\*\*SLE\*\*\* sera, suggesting that the mimotope is shared by ds and ssDNAs as well as native RNA, whereas denatured RNA was not observed to inhibit the binding. The peptide was also able to elicit an immune response in rabbits and the anti-peptide rabbit serum was observed to cross-react with the peptide, ss and dsDNAs, and ss and dsDNAs could inhibit the binding of the anti-peptide serum and the peptide. However, the inhibition was not obtained with RNA. Our findings demonstrate the potential of the peptide mimic in diagnostic tests of \*\*\*SLE\*\*\*, and in the investigation of anti-DNA antibody origin and of DNA-anti-DNA antibody interaction.

L14 ANSWER 7 OF 25 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE

5

AN 2001:152692 BIOSIS

DN PREV200100152692

TI Isolation of human anti-idiotypes broadly cross reactive with \*\*\*anti\*\*\* - \*\*\*dsDNA\*\*\* \*\*\*antibodies\*\*\* from patients with Systemic lupus erythematosus.

AU Zhang, W.; Winkler, T.; Kalden, J. R.; Reichlin, M. (1)

CS (1) Oklahoma Medical Research Foundation, 825 N.E. 13th Street, Oklahoma City, OK, 73104: morris-reichlin@omrf.ouhsc.edu USA

SO Scandinavian Journal of Immunology, (February, 2001) Vol. 53, No. 2, pp. 192-197. print.

ISSN: 0300-9475.

DT Article

LA English

SL English

AB Antibodies to double stranded (ds)DNA play a central role in clinical diagnosis and disease expression in Systemic lupus erythematosus ( \*\*\*SLE\*\*\* ). This paper describes the isolation of anti-idiotypic reagents (anti/antidsDNA) from four \*\*\*SLE\*\*\* sera and the demonstration of broad and quantitatively similar cross reactivity to both polyclonal and monoclonal \*\*\*anti\*\*\* - \*\*\*dsDNA\*\*\* \*\*\*antibodies\*\*\* isolated from \*\*\*SLE\*\*\* patients. Seven \*\*\*affinity\*\*\* -purified polyclonal and three monoclonal human anti-dsDNA preparations reacted preferentially with anti-idiotypic F(ab')2 coated plates compared to normal immunoglobulin (Ig)G F(ab')2 coated plates in ELISA. In contrast, autoantibodies of other specificities (anti-Ro/SSA, anti-La/SSB, and anti-U1RNP) reacted equally with anti/anti-dsDNA F(ab')2 and normal IgG F(ab')2 coated plates. Such anti-idiotypic antibodies could play a significant role in the regulation of \*\*\*anti\*\*\* - \*\*\*dsDNA\*\*\* \*\*\*antibody\*\*\* levels in \*\*\*SLE\*\*\*.

L14 ANSWER 8 OF 25 CAPLUS COPYRIGHT 2002 ACS

AN 2001:424468 CAPLUS

DN 136:133432

TI Development of single-chain Fv fragments from a human anti-double-stranded DNA antibody to study the influence of somatic mutations on antigen binding

AU Kersten, B.; Niemann, B.; Jahn, S.

CS Department of Dermatology, Medical Faculty (Charite), Humboldt-University Berlin, Berlin, Germany

SO Experimental and Clinical Immunogenetics (2001), 18(2), 96-99  
 CODEN: ECIME4; ISSN: 0254-9670

PB S. Karger AG  
 DT Journal  
 LA English  
 AB The monoclonal IgG anti-double-stranded (ds) DNA antibody 32B9, obtained from a patient with systemic lupus erythematosus, was found to be encoded by somatically mutated Ig genes. We examined the input of several somatic mutations into antibody specificity and \*\*\*affinity\*\*\*. Five single-chain (s.c.) Fv fragments [variable domain of the heavy chain (VH)-linker-variable domain of the light chain (VL)] derived from 32B9 were constructed and expressed in *Escherichia coli*. These scFv fragments contained VH or VL fragments, differing in the somatic mutation pattern. The antigen binding features of the 32B9 IgG were compared with the corresponding scFv fragments, and the binding to DNA of all fragments was analyzed by ELISA. Binding constants to dsDNA were determined by surface plasmon resonance and ELISA. The scFv 32B9 reflected the binding features of the 32B9 IgG. Independently of the somatic mutations, all scFv fragments bound to dsDNA in ELISA. The \*\*\*affinity\*\*\* data indicated that the mutations studied had only a marginal effect on \*\*\*affinity\*\*\* maturation of the 32B9. We discuss the approach to constructing scFv fragments as a tool to study autoantibody maturation.

RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 9 OF 25 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.  
 AN 2000308160 EMBASE  
 TI Histone-containing immune complexes are to a large extent responsible for anti-dsDNA reactivity in the Farr assay of active \*\*\*SLE\*\*\* patients.  
 AU Hylkema M.N.; Van Bruggen M.C.J.; Ten Hove T.; De Jong J.; Swaak A.J.G.; Berden J.H.M.; Smeenk R.J.T.  
 CS R.J.T. Smeenk, Department of Autoimmune Diseases, CLB, Plesmanlaan 125,  
 NL-1066 CX Amsterdam, Netherlands. smeenk@clb.nl  
 SO Journal of Autoimmunity, (2000) 14/2 (159-168).  
 Refs: 31  
 ISSN: 0896-8411 CODEN: JOAUPE  
 CY United Kingdom  
 DT Journal; Article  
 FS 026 Immunology, Serology and Transplantation  
 028 Urology and Nephrology  
 LA English  
 SL English  
 AB Increased titres of \*\*\*anti\*\*\* - \*\*\*dsDNA\*\*\* \*\*\*antibodies\*\*\*, especially if of high avidity, are associated with renal exacerbations in patients with systemic lupus erythematosus (\*\*\*SLE\*\*\*). One of the most reliable assays to measure \*\*\*anti\*\*\* - \*\*\*dsDNA\*\*\* \*\*\*antibodies\*\*\*, the Farr assay, is believed to detect preferentially high avidity antibodies. Purified non-complexed monoclonal antibodies (mAbs) against nucleosomes, obtained from mice with \*\*\*SLE\*\*\*, are not reactive in the Farr assay, but can become so once complexed to nucleosomes. These Farr-positive, nucleosome containing, immune complexes were also able to bind in vivo to the glomerular basement membrane (GBM), predominantly via heparan sulphate (HS). To evaluate whether in \*\*\*SLE\*\*\* patients the same kind of immune complexes are responsible for Farr reactivity, IgG from serum or plasma was isolated under dissociating and physiological conditions. We observed that after purification under dissociating conditions, Farr reactivity was significantly decreased ( $P < 0.0001$ ) in contrast to reactivity with histones and two 'control' antigens: Epstein Barr Virus (EBV) and Ro/SS-A. Reactivity with nucleosomes also decreased after purification, although to a lesser extent. Plasma purified under physiological conditions showed no decrease in Farr reactivity. The importance of histones for the generation of immune complexes is supported by the two following observations. Firstly, the presence of histones could be demonstrated in serum and plasma of \*\*\*SLE\*\*\* patients but not in serum of healthy controls or in IgG preparations purified under dissociating conditions. Secondly, Farr reactivity of purified IgG preparations could be restored by addition of purified histones. From these studies we conclude that histones containing immune complexes are responsible for a large part of the Farr reactivity in active \*\*\*SLE\*\*\*, and are therefore indirectly implicated in the pathogenesis of lupus nephritis. (C) 2000 Academic Press.

L14 ANSWER 10 OF 25 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE  
 6  
 AN 1999:510853 BIOSIS  
 DN PREV199900510853  
 TI Bcl-2 leads to expression of anti-DNA B cells but no nephritis: A model for a clinical subset.  
 AU Kuo, Philip; Bynoe, Margaret S.; Wang, Chuansheng; Diamond, Betty (1)  
 CS (1) Department of Microbiology and Immunology, 1300 Morris Park Avenue, Room 405, Bldg. Forchheimer, Bronx, NY, 10461 USA  
 SO European Journal of Immunology, (Oct., 1999) Vol. 29, No. 10, pp. 3168-3178.  
 ISSN: 0014-2980.  
 DT Article  
 LA English  
 SL English  
 AB Transgenic mice expressing anti-DNA antibodies have been extensively studied as a model for understanding B cell regulation in systemic lupus erythematosus (\*\*\*SLE\*\*\*). BALB/c mice transgenic for the R4A-gamma2b heavy chain of an anti-double-stranded DNA (dsDNA) antibody produce two populations of high-\*\*\*affinity\*\*\* anti-dsDNA B cells, one deleted,

and the other anergized. We generated double-transgenic BALB/c mice expressing both the R4A-gamma2b heavy chain and the anti-apoptotic bcl-2 gene in the B cell compartment to study whether bcl-2 overexpression differentially affected anergic and deleted B cells. The double-transgenic mice (R4A/bcl-2) express elevated serum titers of both high- and low-\*\*\*affinity\*\*\* \*\*\*anti\*\*\* - \*\*\*dsDNA\*\*\* \*\*\*antibodies\*\*\* and display rescue of autoreactive B cells that are normally either deleted or anergized. Despite the presence of \*\*\*anti\*\*\* - \*\*\*dsDNA\*\*\* \*\*\*antibodies\*\*\* in their serum, R4A/bcl-2-transgenic mice do not develop nephritis, demonstrating that overexpression of bcl-2 is not by itself sufficient to allow disease progression. This phenotype resembles that of some \*\*\*SLE\*\*\* patients who have high titers of anti-DNA antibodies without nephritis.

L14 ANSWER 11 OF 25 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE

7  
 AN 2000:90300 BIOSIS  
 DN PREV20000090300  
 TI Heterogeneity of \*\*\*anti\*\*\* - \*\*\*dsDNA\*\*\* \*\*\*antibodies\*\*\* in their cross-reaction with ribosomal P protein.  
 AU Takeda, Isao; Rayno, Kim; Wolfson-Reichlin, Marianne; Reichlin, Morris (1)  
 CS (1) Oklahoma Medical Research Foundation, 825 Northeast 13 Street, Oklahoma City, OK, 73104 USA  
 SO Journal of Autoimmunity, (Dec., 1999) Vol. 13, No. 4, pp. 423-428.  
 ISSN: 0896-8411.  
 DT Article  
 LA English  
 SL English  
 AB We have investigated the possible cross-reaction of \*\*\*anti\*\*\* - \*\*\*dsDNA\*\*\* \*\*\*antibodies\*\*\* with ribosomal P peptide for several reasons. First, the antibodies frequently occur together, and secondly, they vary similarly with disease activity. Human polyclonal \*\*\*anti\*\*\* - \*\*\*dsDNA\*\*\* \*\*\*antibodies\*\*\* were \*\*\*affinity\*\*\* purified from eight patients and anti-ribosomal P antibodies from two patients with systemic Lupus erythematosus (\*\*\*SLE\*\*\*) who had high titers of anti-dsDNA as well as anti-ribosomal P antibodies. Nine of the 10 sera were totally specific in their reactivity with their cognate antigens. In only one patient did we find a subpopulation of antibodies which cross-reacted with both dsDNA and the carboxyl terminal 22 amino acid peptide. Our results indicate that \*\*\*anti\*\*\* - \*\*\*dsDNA\*\*\* \*\*\*antibodies\*\*\* are heterogeneous and usually do not cross-react with the carboxyl terminal P peptide, but on occasion (1/10) a patient will produce \*\*\*anti\*\*\* - \*\*\*dsDNA\*\*\* \*\*\*antibodies\*\*\* cross-reactive with the carboxyl terminal P peptide.

L14 ANSWER 12 OF 25 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 8  
 AN 1999180779 EMBASE  
 TI Initiation of systemic autoimmunity and sequence specific anti-DNA autoantibodies.  
 AU Radic M.Z.; Cocco B.A.; Seal S.N.  
 CS M.Z. Radic, Dept. of Microbiology and Immunology, MCP Hahnemann University, Philadelphia, PA 19129, United States  
 SO Critical Reviews in Immunology, (1999) 19/2 (117-126).  
 Refs: 76  
 ISSN: 1040-8401 CODEN: CCRIDE  
 CY United States  
 DT Journal; General Review  
 FS 005 General Pathology and Pathological Anatomy  
 026 Immunology, Serology and Transplantation  
 LA English  
 SL English  
 AB Antibodies to double-stranded DNA (dsDNA) are a defining feature of Systemic Lupus Erythematosus (\*\*\*SLE\*\*\*). The molecular characterization of anti-dsDNA autoantibodies reveals that they are actively selected for binding to antigen. Evidence for antigen selection includes the use of suitable rearrangement products, the switching of IgM isotype to IgG, and the acquisition of somatic mutations that raise the \*\*\*affinity\*\*\* for dsDNA. Through a process of specificity maturation, \*\*\*anti\*\*\* - \*\*\*dsDNA\*\*\* \*\*\*antibodies\*\*\* can arise from anti-single stranded DNA (ssDNA) antibodies that also occur in nonautoimmune individuals. To clarify circumstances leading to the initiation of systemic autoimmunity, we compare features of immune responses to nucleic acids that operate before and after disease develops. Evidence indicating that \*\*\*anti\*\*\* - \*\*\*dsDNA\*\*\* \*\*\*antibodies\*\*\* bind with DNA sequence preference is highlighted to propose that sequence-specific \*\*\*anti\*\*\* - \*\*\*dsDNA\*\*\* \*\*\*antibodies\*\*\* may be induced by an infectious agent and in turn may extend the response to endogenous nuclear antigens. Thus, sequence-specific anti-dsDNA B cells may provide an important stimulus to break the tolerance to self.

L14 ANSWER 13 OF 25 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.  
 AN 97159521 EMBASE  
 DN 1997159521  
 TI A case report of typical scleroderma accompanied with serum abnormalities characteristic of \*\*\*SLE\*\*\* during the course.  
 AU Nishiyama S.; Kakiyama H.; Miyawaki S.  
 CS S. Nishiyama, Center for Adult Diseases Kurashiki, Minami Kurashiki Hospital, Kurashiki-city, Japan  
 SO Ryumachi, (1997) 37/1 (24-29).  
 Refs: 15  
 ISSN: 0300-9157 CODEN: RYMCAF

CY Japan  
DT Journal; Article  
FS 031 Arthritis and Rheumatism  
LA Japanese  
SL English; Japanese

AB A 40-year-old woman had complained of cyanosis induced by cold exposure from the age of 26. When she was 32 years old, Raynaud's phenomenon occurred. She developed diffuse cutaneous sclerosis affecting the upper limbs, face and trunk, digital pitting scar, flexion contractures of hands, dilatation of lower esophagus and pulmonary fibrosis, and she was diagnosed as scleroderma. Laboratory findings revealed positive anti-topoisomerase I antibody and hypergammaglobulinemia (IgG 2,782, IgA 632, IgM 146 mg/dl). However, serum complement levels were normal and anti-DNA antibodies measured by radioimmunoassay (RIA) were negative. Initial dose of oral prednisolone was 30 mg/day and afterwards 5 mg/day of prednisolone was maintained. At the age of 36, scleroderma and contraction of hands were progressed, and telangiectasias appeared on her chest at the age of 36. Laboratory tests revealed hypocomplementemia (C3 27, C4 9 mg/dl, CH50 16 U/ml) and high titers, more than 100 U/ml, of anti-DNA antibodies measured by RIA. Clinical evidence suggestive of \*\*\*SLE\*\*\* could not be found. Reexamination of previous sera by enzyme immunoassay, in which anti-DNA antibody could not be detected by RIA, clarified the presence of IgG \*\*\*anti\*\*\* - \*\*\*dsDNA\*\*\* \*\*\*antibodies\*\*\*. It was considered that there existed low avidity/ \*\*\*affinity\*\*\* of \*\*\*anti\*\*\* - \*\*\*dsDNA\*\*\* \*\*\*antibodies\*\*\* at first, and afterwards high avidity/ \*\*\*affinity\*\*\* of \*\*\*anti\*\*\* - \*\*\*dsDNA\*\*\* \*\*\*antibodies\*\*\* appeared. Increasing of oral prednisolone up to 30 mg/day normalized serum complements and decreased titers of anti-DNA antibodies. She had not developed any clinical evidence that suspected \*\*\*SLE\*\*\* throughout the course.

L14 ANSWER 14 OF 25 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE

9  
AN 1996:284323 BIOSIS  
DN PREV199699006679  
TI The double edged sword of the immune response: Mutational analysis of a murine anti-pneumococcal, anti-DNA antibody.  
AU Puttermann, Chaim; Limpasathikul, Wacharee; Edelman, Morris; Diamond, Betty (1)  
CS (1) Dep. Microbiol. Immunology, Albert Einstein Coll. Med., 1300 Morris Park Ave., Bronx, New York, 10461 USA  
SO Journal of Clinical Investigation, (1996) Vol. 97, No. 10, pp. 2251-2259. ISSN: 0021-9738.  
DT Article  
LA English

AB Anti-double-stranded (ds) DNA antibodies are not only an important diagnostic marker for \*\*\*SLE\*\*\*, but also play an important role in tissue injury. Microbial antigen may be a stimulus for the production of these antibodies. We isolated 99D.7E, an IgG2b monoclonal antibody from a nonautoimmune BALB/c mouse that is cross-reactive with both dsDNA and phosphorylcholine, the dominant hapten on the pneumococcal cell wall. While partially protective against a bacterial challenge, 99D.7E is also pathogenic to the kidney. To identify those molecular motifs that confer on anti-PC antibodies the potential for autoreactivity, we created a panel of 99D.7E mutants with single amino acid substitutions in the heavy chain, and examined the changes in antigen binding and renal deposition. Our results support the hypothesis that charge and \*\*\*affinity\*\*\* for dsDNA are not adequate predictors of the pathogenicity of anti-DNA antibodies. Differential renal damage from \*\*\*anti\*\*\* - \*\*\*dsDNA\*\*\* \*\*\*antibodies\*\*\* may be due to differences in fine specificity, rather than differential \*\*\*affinity\*\*\* for dsDNA. Importantly, high \*\*\*affinity\*\*\* IgG antibodies cross-reactive with bacterial and self antigen exist and can display pathogenic potential, suggesting that defects in peripheral regulation of B cells, activated by foreign antigen but cross-reactive with self antigen, might lead to autoimmune disorders.

L14 ANSWER 15 OF 25 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE

10  
AN 1997:43775 BIOSIS  
DN PREV199799335763  
TI Autoantibodies to double-stranded (ds)DNA immunoprecipitate 18S ribosomal RNA by virtue of their interaction with ribosomal protein S1 and suppress in vitro protein synthesis.  
AU Tsuzaka, K.; Winkler, T. H.; Kalden, J. R.; Reichlin, M. (1)  
CS (1) Oklahoma Med. Res. Foundation, 825 N.E. 13th St., Oklahoma City, OK 73104 USA  
SO Clinical and Experimental Immunology, (1996) Vol. 106, No. 3, pp. 504-508. ISSN: 0009-9104.  
DT Article  
LA English  
AB We report that four systemic lupus erythematosus ( \*\*\*SLE\*\*\* ) patient sera containing \*\*\*anti\*\*\* - \*\*\*dsDNA\*\*\* \*\*\*antibodies\*\*\*, three \*\*\*affinity\*\*\* -purified anti-dsDNA IgG, and a human anti-dsDNA MoAb (33.H11) immunoprecipitate 18S ribosomal RNA from DNase-treated 32P-labelled MOLT4 cell extract. This 18S RNA precipitation was inhibited completely by preincubating 33.H11 with calf thymus dsDNA or the recombinant human ribosomal protein S1, which was reported to cross-react with \*\*\*anti\*\*\* - \*\*\*dsDNA\*\*\* \*\*\*antibodies\*\*\* (J Immunol 1996; 156:1668-75). Whole IgG from three \*\*\*SLE\*\*\* sera with \*\*\*anti\*\*\* - \*\*\*dsDNA\*\*\* \*\*\*antibodies\*\*\*, 33.H11, and three \*\*\*affinity\*\*\* -purified anti-dsDNA IgG inhibited in vitro translation of globin mRNA

(percent inhibition was 36-50%). This translation inhibition by anti-dsDNA antibodies was enhanced (67-79%) when the reticulocyte lysate was treated with DNase. Suppression of protein synthesis could be a pathogenic mechanism of \*\*\*anti\*\*\* - \*\*\*dsDNA\*\*\* \*\*\*antibodies\*\*\*, since it has also been shown that anti-dsDNA penetrates living cells (J Immunol 1995; 154:4857-64) in culture.

L14 ANSWER 16 OF 25 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE

11  
AN 1996:220505 BIOSIS  
DN PREV199698776634  
TI The expression of acidic ribosomal phosphoproteins on the surface membrane of different tissues in autoimmune and normal mice which are the target molecules for anti-double-stranded DNA antibodies.  
AU Sun, K.-H.; Lku, W.-T.; Tang, S.-J.; Tsai, C.-Y.; Hsieh, S.-C.; Wu, T.-H.; Han, S.-H.; Yu, C.-L. (1)  
CS (1) Section Allergy, Immunol. Rheumatol., Dep. Med., Veterans General Hosp.-Taipei, National Yang-Ming Univ., 201 Sec. 2, Shih-Pai Rd., Taipei 11217 Taiwan  
SO Immunology, (1996) Vol. 87, No. 3, pp. 362-371. ISSN: 0019-2805.  
DT Article  
LA English  
AB \*\*\*Affinity\*\*\* -purified polyclonal anti-double-stranded DNA ( \*\*\*anti\*\*\* - \*\*\*dsDNA\*\*\* ) \*\*\*antibodies\*\*\* from patients with systemic lupus erythematosus ( \*\*\*SLE\*\*\* ) exert a cytostatic effect on cultured rat glomerular mesangial cells (MC). The cognate antigens expressed on the surface of MC have been proved to be acidic ribosomal phosphoproteins (P proteins) in our previous study. The mesangial cytostatic effect of \*\*\*anti\*\*\* - \*\*\*dsDNA\*\*\* \*\*\*antibodies\*\*\* is attributed to the cross-reactivity of the antibodies with membrane-expressed P proteins, but not to the effect of minute amounts of anti-ribosomal P proteins antibodies contained in the anti-dsDNA preparations. Immunofluorescence staining of the native cells demonstrated that \*\*\*anti\*\*\* - \*\*\*dsDNA\*\*\* \*\*\*antibodies\*\*\* bound to the surface of rat mesangial cells, rat brain astrocytes (RBA-1) and mouse fibroblasts (3T3). \*\*\*Anti\*\*\* - \*\*\*dsDNA\*\*\* \*\*\*antibodies\*\*\* also exert potent cytostatic effects on these cells in a dose-dependent manner. In addition, the plasma membranes of different cell lines and tissues from normal and autoimmune mice were isolated and probed by \*\*\*anti\*\*\* - \*\*\*dsDNA\*\*\* \*\*\*antibodies\*\*\* in Western blot analysis. We found the actively proliferating cells such as MC, RBA-1 and 3T3 may express both P0 (38 000 MW) and P1 (19 000 MW) on the surface membrane. In addition, the kidney, liver and spleen from either autoimmune MRL-lpr/lpr or BALB/c mice may constantly express P0 protein, but the expression of P1 is inconsistent. In contrast, brain and muscle from either mice failed to express P proteins on their surface. Unexpectedly, a high molecular weight substance (larger than 205 000 MW) with unknown nature appears in the membrane of brain and muscle tissues in both mice. Immunoprecipitation of the surface-biotinylated MC-lysate by \*\*\*anti\*\*\* - \*\*\*dsDNA\*\*\* \*\*\*antibodies\*\*\* further confirmed that P1 (19 000 MW) and P2 (17 000 MW) are really expressed on the cell surface. These results suggest that P proteins expressed on the surface of different tissues become the targets for \*\*\*anti\*\*\* - \*\*\*dsDNA\*\*\* \*\*\*antibodies\*\*\* mediating pleomorphic tissue damage in patients with \*\*\*SLE\*\*\*.

L14 ANSWER 17 OF 25 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

AN 96144011 EMBASE  
DN 1996144011  
TI High-avidity anti-DNA antibody removal from the serum of systemic lupus erythematosus patients by adsorption using dextran sulfate cellulose columns.  
AU Matsuki Y.; Suzuki K.; Kawakami M.; Ishizuka T.; Kawaguchi Y.; Hidaka T.; Nakamura H.  
CS Internal Medicine I, National Defense Medical College, 3-2 Namiki, Tokorozawa, Saitama 359, Japan  
SO Journal of Clinical Apheresis, (1996) 11/1 (30-35). ISSN: 0733-2459 CODEN: JCAPE5  
CY United States  
DT Journal; Article  
FS 025 Hematology  
026 Immunology, Serology and Transplantation  
LA English  
SL English  
AB The purpose of this study is to determine whether immunoabsorption treatment using a dextran sulfate (DS) column can remove high-avidity anti-double-stranded DNA ( \*\*\*anti\*\*\* - \*\*\*dsDNA\*\*\* ) \*\*\*antibody\*\*\* from the blood of patients with systemic lupus erythematosus ( \*\*\*SLE\*\*\* ). Before and after each immunoabsorption therapy routine, titers of the high-avidity \*\*\*anti\*\*\* - \*\*\*dsDNA\*\*\* \*\*\*antibody\*\*\* of 11 \*\*\*SLE\*\*\* patients were measured by using a newly developed assay kit to exclusively detect high avidity anti-DNA antibody. Patients with active \*\*\*SLE\*\*\* showed significantly higher titers of high-avidity antibody than did those with inactive \*\*\*SLE\*\*\*, and their titers were significantly reduced by immunoabsorption procedures. Removal of high avidity antibodies in vitro was also confirmed by mixing patients' sera and DS gel. Immunoabsorption therapy using DS columns is effective in the removal of high-avidity \*\*\*anti\*\*\* - \*\*\*dsDNA\*\*\* \*\*\*antibodies\*\*\* that are closely associated with pathogenicity in \*\*\*SLE\*\*\*.

L14 ANSWER 18 OF 25 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS  
INC.DUPLICATE  
12

AN 1995:392870 BIOSIS

DN PREV199598407170

TI \*\*\*Anti\*\*\* - \*\*\*dsDNA\*\*\* \*\*\*antibodies\*\*\* cross-react with ribosomal P proteins expressed on the surface of glomerular mesangial cells to exert a cytostatic effect.

AU Sun, K.-H.; Liu, W.-T.; Tsai, C.-Y.; Tang, S.-J.; Han, S.-H.; Yu, C.-L.  
(1)

CS (1) Section Allergy Immunology Rheumatology, Dep. Med., Veterans General Hosp.-Taipei, National Yang-Ming Univ. Sch. Med., no. 201 Section 2, Shih-Pai Road, Taipei 11217 Taiwan

SO Immunology, (1995) Vol. 85, No. 2, pp. 262-269.  
ISSN: 0019-2805.

DT Article

LA English

AB \*\*\*Affinity\*\*\* -purified human polyclonal anti-double-stranded DNA antibodies (anti-dsDNA) exerted a cytostatic effect towards human and rat glomerular mesangial cells (MC). In order to identify the cognate antigens for anti-dsDNA on the surface of MC, we used these autoantibodies to probe a human renal lambda-gt11 cDNA expression library. Two cDNA clones encoding the cognate proteins for the autoantibodies were isolated. Sequencing analysis of the two cDNA showed that they had 98-6% homology with the gene of the P-0 and 99.2% homology with the gene of the PI human acidic ribosomal phosphoproteins (P protein). Two galactosidase fusion proteins (125000 and 150 000 MVV) derived from the two cDNA inserts expressed in lysogenic Escherichia coli Y1089 could react with the original screening antibodies in an immunoblotting analysis. After transformation and expression of the full-length P-1 clone in prokaryotic cells, the purified P-1 protein was able to react with anti-dsDNA. In a cross-inhibition experiment, the dsDNA binding activity of anti-dsDNA was inhibited by a synthetic polypeptide corresponding to the carboxyterminal 20 amino acids of P protein and purified P-1 protein in a dose-dependent manner, but this was less potent than the inhibition caused by calf thymus dsDNA. By use of well-defined systemic lupus erythematosus ( \*\*\*SLE\*\*\* ) sera, we found only sera containing a high titre of anti-dsDNA activity ( gt 300 IU/ml) reacted with P-1 of rat MC lysate. Furthermore, the 38 000 and 19 000 MW macromolecules were proved to be the cognate antigens for anti-dsDNA expression on the surface of the MC, by Western blot of the MC plasma membrane lysates. These results suggest that anti-dsDNA may cross-react with ribosomal P proteins expressed on the surface of the MC and exert cytostasis towards these cells.

L14 ANSWER 19 OF 25 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS  
INC.DUPLICATE  
13

AN 1993:523307 BIOSIS

DN PREV199396136714

TI Antibodies to dsDNA are produced during primary BK virus infection in man, indicating that \*\*\*anti\*\*\* - \*\*\*dsDNA\*\*\* \*\*\*antibodies\*\*\* may be related to virus replication in vivo.

AU Fredriksen, Knut (1); Skogsholm, A.; Flaegstad, T.; Traavik, T.; Rekvig, O. P.

CS (1) Dep. Virol., Inst. Med. Biol., Univ. Tromsø, N-9037 Tromsø Norway

SO Scandinavian Journal of Immunology, (1993) Vol. 38, No. 4, pp. 401-406.  
ISSN: 0300-9475.

DT Article

LA English

AB Experimental immunizations with both the Polyomavirus BK and with the isolated viral genomic dsDNA regularly induce antibodies with a relative \*\*\*affinity\*\*\* for BK virus dsDNA. In the present study we demonstrate that the anti-dsDNA responses to BK virus in experimental animals also appear during natural BK virus infection in man. Fifty-nine children were examined over time for serological signs of primary BK virus infection. Of eight children found to undergo primary infection with BK virus, anti-BK dsDNA antibodies appeared in all. In 4 of the 8 patients the antibodies cross-reacted significantly with mammalian dsDNA, and weak cross-reactions were also noted in at least three other patients. The antibodies resembled those induced in the experimental model with regard to their relative \*\*\*affinity\*\*\* for BK dsDNA. In contrast, most, but not all, \*\*\*anti\*\*\* - \*\*\*dsDNA\*\*\* \*\*\*antibodies\*\*\* from 10 \*\*\*SLE\*\*\* patients cross-reacted extensively with dsDNA from viral and mammalian origin. Thus, a dsDNA virus like BK virus may provoke immunological intolerance to dsDNA, but, with qualities different from those produced during \*\*\*SLE\*\*\*. The present observations demonstrate that induction of \*\*\*anti\*\*\* - \*\*\*dsDNA\*\*\* \*\*\*antibodies\*\*\* is not restricted to experimental immunization of animals, but does also take place in humans during naturally acquired BK virus infection. The relevance of this model for the spontaneous production of \*\*\*anti\*\*\* - \*\*\*dsDNA\*\*\* \*\*\*antibodies\*\*\* is discussed.

L14 ANSWER 20 OF 25 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS  
INC.DUPLICATE  
14

AN 1993:275060 BIOSIS

DN PREV199396005285

TI Production and analysis of the IgG monoclonal anti-DNA antibodies from systemic lupus erythematosus ( \*\*\*SLE\*\*\* ) patients.

AU Ehrenstein, M.; Longhurst, C.; Isenberg, D. A. (1)

CS (1) Dep. Rheumatol. Res., Univ. Coll. Midx Hosp. Med. Sch., London W1P 9PG UK

SO Clinical and Experimental Immunology, (1993) Vol. 92, No. 1, pp. 39-45.

ISSN: 0009-9104.

DT Article

LA English

AB This study compares recently devised methods for producing IgG anti-DNA MoAbs from patients with \*\*\*SLE\*\*\* and analyses the antibodies generated from one patient at different phases of disease. Lymphocytes from \*\*\*SLE\*\*\* patients were transformed with Epstein-Barr virus (EBV) and/or fused with a heteromyeloma cell line, CB-F7. Direct fusion with CB-F7 resulted in the highest proportion of IgG-secreting lines, whereas EBV transformation resulted in a high percentage of IgM-secreting lines. Using direct fusion, five IgM anti-DNA antibody-secreting hybridomas were generated using lymphocytes from a patient with relatively inactive \*\*\*SLE\*\*\*. Six months later when the disease was active, only IgG anti-DNA antibodies were produced. The antigen-binding patterns of the MoAbs were analyzed. Only one of the IgM anti-DNA antibodies reacted with dsDNA by ELISA and none by Crithidia immunofluorescence, whereas two of the IgG antibodies reacted with dsDNA by ELISA and Crithidia but did not bind to ssDNA. Only the two IgG high \*\*\*affinity\*\*\* \*\*\*anti\*\*\* - \*\*\*dsDNA\*\*\* \*\*\*antibodies\*\*\* bound to histones, and this was enhanced by added DNA, whereas three IgM antibodies bound to cardiolipin. This study supports the notion that MoAbs derived from a patient with \*\*\*SLE\*\*\* represent those found in the serum of \*\*\*SLE\*\*\* patients at different stages of disease activity. The binding to histones by the two IgG \*\*\*anti\*\*\* - \*\*\*dsDNA\*\*\* \*\*\*antibodies\*\*\* supports the recently expressed view that antibodies binding DNA/histone may be important in the pathogenesis of \*\*\*SLE\*\*\*.

L14 ANSWER 21 OF 25 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS  
INC.DUPLICATE  
15

AN 1992:410640 BIOSIS

DN BA94:73840

TI ANALYSIS OF IMMUNOGLOBULIN VARIABLE REGION GENES FROM HUMAN IGG ANTI-DNA HYBRIDOMAS.

AU WINKLER T H; FEHR H; KALDEN J R

CS INSTITUT F. KLINISCHE IMMUNOLOGIE RHEUMATOLOGIE, KRANKENHAUSSTRASSE 12, D-8520 ERLANGEN, GER.

SO EUR J IMMUNOL, (1992) 22 (7), 1719-1728.

CODEN: EJIMAF. ISSN: 0014-2980.

FS BA; OLD

LA English

AB The molecular mechanisms leading to anti-double-stranded (ds)DNA antibody production in systemic lupus erythematosus ( \*\*\*SLE\*\*\* ) are poorly understood. We describe here the immunoglobulin variable region genes of six human hybridomas secreting IgG \*\*\*anti\*\*\* - \*\*\*dsDNA\*\*\* \*\*\*antibodies\*\*\* derived from three \*\*\*SLE\*\*\* patients. The monoclonal IgG \*\*\*anti\*\*\* - \*\*\*dsDNA\*\*\* \*\*\*antibodies\*\*\* have been shown to be of high \*\*\*affinity\*\*\* and no multireactivity was observed (Winkler et al., Clin. Exp. Immunol., 1991, 85: 379). The comparison of the variable region genes expressed in the hybridomas with known germ-line genes as well as with the germ-line counterparts from one patient shows that the VH and VL sequences are somatically mutated. The pattern and extent of the observed somatic mutations are suggestive for an antigen-driven selection of at least four of these B cell clones. Several VH and VL genes used by the hybridomas were found to be expressed in the natural antibody repertoire, in the restricted fetal repertoire and in B cell malignancies expressing the CD5 antigen.

L14 ANSWER 22 OF 25 CAPLUS COPYRIGHT 2002 ACS

AN 1992:569296 CAPLUS

DN 117:169296

TI Detection of autoantibody to the 19kD centromere antigen using immunoblotting in connective tissue diseases

AU Takashina, Naoya; Kondo, Hirobumi; Kashiwazaki, Sadao

CS Sch. Med., Kitasato Univ., Sagamihara, Japan

SO Kitasato Igaku (1992), 22(1), 84-92

CODEN: KIIGDP. ISSN: 0385-5449

DT Journal

LA English

AB Sera were tested from patients, including 113 with systemic sclerosis (SSc), 44 with sclerodactyly and Raynaud's phenomenon (SR), 100 with systemic lupus erythematosus ( \*\*\*SLE\*\*\* ), 47 with mixed connective tissue disease, and 84 with primary Sjogren's syndrome (SS), for anticentromere antibodies (ACA) by immunoblotting, using nuclear-enriched sonicate of HeLa cells and \*\*\*affinity\*\*\* purified centromere antigen. Forty-one sera recognized a 19kD polypeptide when immunoblotted against both nuclear-enriched sonicate and purified antigen. ACA were also detected by immunofluorescence on chromosome spreads of Wil-2 cells in all these sera. Two of them did not show a discrete speckled pattern on immunofluorescence of Hep-2 cells due to masking phenomena with coexisting antinuclear antibodies (ANA). Three ACA pos. sera failed to recognize the 19kD polypeptide. Six of the 44 sera with ACA contained coexisting other ANA (one with anti-topoisomerase I, 2 with anti-U1RNP, 2 with anti-ENA that could not be further characterized, and 1 with \*\*\*anti\*\*\* - \*\*\*dsDNA\*\*\* \*\*\*antibodies\*\*\* ). ACA occasionally coexist with other ANA. Immunoblotting anal. thus may be useful for the detection of ACA coexisting with other ANA. ACA were present in 16 (14%) of SSc, 19 (43%) of SR, 2 (2%) of \*\*\*SLE\*\*\*, and 7 (8%) of primary SS. Raynaud's phenomenon was found in 43 (98%) of the ACA pos. patients, though the other features of CREST syndrome (calcinosis, esophageal involvement, sclerodactyly, and telangiectasia) were less frequently seen (range:

14%-52%). ACA may not be disease specific antibodies and are assocd. with Raynaud's phenomenon.

L14 ANSWER 23 OF 25 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE  
18  
AN 1989:427475 BIOSIS  
DN BA88:85733  
TI BINDING PROPERTIES OF HUMAN ANTI-DNA ANTIBODIES TO CLONED HUMAN DNA FRAGMENTS.  
AU SANO H; TAKAI O; HARATA N; YOSHINAGA K; KODAMA-KAMADA I; SASAKI T  
CS BIOTECHNOL. INST., AKITA PREFECT. COLL. AGRIC., OHGATA, AKITA 010-04, JPN.  
SO SCAND J IMMUNOL., (1989) 30 (1), 51-64.  
CODEN: SJIMAX. ISSN: 0300-9475.  
FS BA; OLD  
LA English  
AB The DNA-anti-DNA antibody immune complexes were isolated from plasma of systemic lupus erythematosus ( "SLE" ) patients and DNA fragments separated from immune complexes were subjected to molecular cloning. The resulting recombinant DNA clones showed a molecular size of 37-79 base pairs, a high guanine and cytosine content, high frequencies of CpG dinucleotides, and palindromic sequences, and also clusters of G + C- and A + T-rich segments. These clones hybridized randomly to total human DNA. The reactivity of dsDNA antibodies, both monoclonal and polyclonal, from "SLE" was examined with a cloned "SLE" antigen DNA. A competitive inhibition assay showed that human monoclonal antibodies had at least one magnitude higher "affinity" to the cloned DNA than to the native DNA fragments. In order to characterize the factors that were recognized by antibodies, human G + C-rich and also A + T-rich 100 bp DNA fragments were cloned, and their base sequence determined. The antibody showed a higher "affinity" to the G + C-rich DNA fragment (71% G + C) than to the A + T-rich DNA fragment (46% G + C). When cytosines in CpG doublets in G + C-rich fragments were methylated (mCpG), the reactivity increased up to 100-fold. The native anti-DNA antibodies from "SLE" patients also showed preferential binding to G + C-rich fragments. These observations suggested that human "anti" - "dsDNA" "antibodies" may recognize some unique structures around the G + C regions or G + C clusters of DNA.

L14 ANSWER 24 OF 25 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE  
17  
AN 1985:251423 BIOSIS  
DN BA79:31419  
TI DETECTION OF MASKED ANTI-DNA ANTIBODIES IN LUPUS SERA BY A MONOCLONAL ANTI-IDIOTYPE.  
AU HALPERN R; SCHIFFENBAUER J; SOLOMON G; DIAMOND B  
CS DEPARTMENT OF MICROBIOLOGY AND IMMUNOLOGY AND OF MEDICINE, ALBERT EINSTEIN COLLEGE OF MEDICINE, BRONX, N. Y. 10461.  
SO J IMMUNOL., (1984) 133 (4), 1852-1856.  
CODEN: JOIMA3. ISSN: 0022-1767.  
FS BA; OLD  
LA English  
AB A monoclonal anti-idiotype 31 to human anti-DNA antibodies was used to detect in serum idiotype-positive antigen-binding antibodies lacking DNA-binding activity as measured by conventional antigen binding assays. Paired serum samples from 13 patients with systemic lupus erythematosus ( "SLE" ) obtained at 2 times in the course of their disease: in each patient, 1 serum sample has anti-DNA activity and the 2nd serum sample has no anti-ds [double stranded] DNA activity detectable by Millipore filter, ELISA [enzyme-linked immunosorbent assay], or Crithidia assay. Reactivity with 3I as detected with a radioimmunoassay (RIA) was present in all 13 sera with anti-dsDNA activity. Six patients showed a decrease in 3I reactivity to normal levels in the 2nd serum sample, in which "anti" - "dsDNA" "antibodies" were not detectable by conventional antigen-binding assays. The other 7 patients' 2nd serum sample continued to show elevated 3I reactivity by RIA even though no anti-dsDNA activity was apparent. When the 3I-reactive antibodies from these latter patients' sera were eluted from a 3I "affinity" column, they revealed DNA-binding activity. dsDNA binding by these sera was apparent when they were displayed on Western blots of isoelectric focusing gels run in 8 M urea and incubated with radiolabeled dsDNA. Thus, the 3I anti-idiotype can detect anti-DNA antibodies in some sera of "SLE" patients that lack anti-DNA activity by ordinary assays. These antibodies may be inhibited in binding dsDNA by excess antigen or autologous anti-idiotype, and their DNA binding activity can be unmasked by procedures promoting immune complex dissociation.

L14 ANSWER 25 OF 25 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE  
18  
AN 1983:207506 BIOSIS  
DN BA75:57506  
TI HIDDEN ANTI DOUBLE STRANDED DNA ANTIBODIES IN AUTO IMMUNE MICE.  
AU FISH F; ZIFF M  
CS DEP. INTERNAL MED., UNIV. TEXAS HEALTH SCIENCE CENT., 5323 HARRY HINES

BLVD., DALLAS, TEX. 75235, USA.  
SO CLIN EXP IMMUNOL., (1982) 49 (3), 587-597.  
CODEN: CEXIAL. ISSN: 0009-9104.  
FS BA; OLD  
LA English  
AB When MRL/l mouse spleen cell culture supernatants were incubated with normal mouse spleen cells, a 2-50-fold increase in anti-dsDNA [double stranded DNA] activity was noted. A smaller increase in anti-ssDNA [single stranded DNA] and no change in anti-TNP antibody activity were observed. This hidden antibody in the MRL/l supernatants could not be revealed by DNAase digestion and could not be absorbed by a DNA cellulose column. Hidden antibody was removed from supernatants by sepharose-anti-Ig. After DNAase digestion of the MRL/l supernatants, hidden anti-dsDNA could not be revealed by incubation with spleen cells. All the hidden activity was excluded by gel filtration on Sephacryl S-300 (MW > 300,000) but was banded in the low density protein area of CsCl- equilibrium density gradients. MRL/l mouse sera had hidden "anti" - "dsDNA" "antibodies". Hidden antibodies were present in both the IgG and IgM classes. The revealed antibodies demonstrated impaired ability to bind Fc specific anti-Ig reagents suggesting that they were partially degraded during the incubation with mouse spleen cells. The hidden anti-dsDNA appears to represent a DNA-anti-dsDNA complex, perhaps of very high "affinity". It may explain why anti-dsDNA but not anti-ssDNA antibodies are of pathological importance in "SLE" [systemic lupus erythematosus].

=> d his  
(FILE 'HOME' ENTERED AT 14:14:50 ON 26 NOV 2002)  
FILE 'BIOSIS, EMBASE, CAPLUS' ENTERED AT 14:30:51 ON 26 NOV 2002  
L1 0 S IMMUNOGENIC VALENCY PLATFORM MOLECULE?  
L2 71 S IMMUNO? (3A) PLATFORM  
L3 1 S L2 AND (SLE OR SYSTEMIC LUPUS ERYTHEMATOSUS)  
L4 3 S L2 AND AFFINITY  
L5 4 S L3 OR L4  
L6 4 DUP REM L5 (0 DUPLICATES REMOVED)  
L7 56 S LJP 394  
L8 40 DUP REM L7 (16 DUPLICATES REMOVED)  
L9 4 S L8 AND AFFINITY?  
L10 1 S NON IMMUNOGENIC VALENCY PLATFORM  
L11 1064 S ANTI-DSDNA ANTIBOD?  
L12 581 S L11 AND SLE  
L13 54 S L12 AND AFFINITY?  
L14 25 DUP REM L13 (29 DUPLICATES REMOVED)  
=> s SLE  
L15 25800 SLE  
=> s valency platform molecule  
L16 2 VALENCY PLATFORM MOLECULE  
=> s valency platform molecule?  
L17 7 VALENCY PLATFORM MOLECULE?  
=> dup rem l17  
PROCESSING COMPLETED FOR L17  
L18 6 DUP REM L17 (1 DUPLICATE REMOVED)  
=> s l18 and l11  
L19 0 L18 AND L11  
=> d bib abs l18  
L18 ANSWER 1 OF 6 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.  
AN 2002:423913 BIOSIS  
DN PREV200200423913  
TI APL immunoreactive peptides, conjugates thereof and methods of treatment for APL antibody-mediated pathologies.  
AU Victoria, Edward Jess (1); Marquis, David Matthew, Jones, David S.; Yu, Lin  
CS (1) San Diego, CA USA  
ASSIGNEE: La Jolla Pharmaceutical Company  
PI US 6410775 June 25, 2002  
SO Official Gazette of the United States Patent and Trademark Office Patents, (June 25, 2002) Vol. 1259, No. 4, pp. No Pagination.  
<http://www.uspto.gov/web/menu/patdata.html>. e-file.  
ISSN: 0098-1133.  
DT Patent  
LA English  
AB aPL analogs that (a) bind specifically to B cells to which an aPL epitope binds and are disclosed. Optimized analogs lack T cell epitope(s) are useful as conjugates for treating aPL antibody-mediated diseases. Conjugates comprising aPL analogs and nonimmunogenic "valency" "platform" "molecules" are provides as are novel nonimmunogenic "valency" "platform" "molecules" and linkers. Methods of preparing and identifying said analogs, methods of treatment using said analogs, methods and compositions for preparing conjugates of said analogs and diagnostic immunoassays for aPL antibodies are disclosed.



=> d bib abs 2-  
L18 HAS NO ANSWERS  
'2-' IS NOT A VALID SEARCH STATUS KEYWORD  
Search status keywords:  
NONE ---- Display only the number of postings.  
STATUS -- Display statistics of the search.  
ENTER SEARCH STATUS OPTION (NONE), STATUS, OR ?;y  
'Y' IS NOT A VALID SEARCH STATUS KEYWORD  
Search status keywords:  
NONE ---- Display only the number of postings.  
STATUS -- Display statistics of the search.  
ENTER SEARCH STATUS OPTION (NONE), STATUS, OR ?;none  
L11 1064 SEA ANTI-DSDNA ANTIBODY?  
L17 7 SEA VALENCY PLATFORM MOLECULE?  
L18 6 DUP REM L17 (1 DUPLICATE REMOVED)  
L19 0 SEA L18 AND L11

=> d bib abs l18 2-  
YOU HAVE REQUESTED DATA FROM 5 ANSWERS - CONTINUE? Y(N);y

L18 ANSWER 2 OF 6 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS  
INC.  
AN 2002:378035 BIOSIS  
DN PREV200200378035  
TI Conjugates comprising galactose alpha1,3 galactosyl epitopes and methods  
of using same.  
AU Jack, Richard M. (1); Jones, David S.; Yu, Lin  
CS (1) Del Mar, CA USA  
ASSIGNEE: La Jolla Pharmaceutical Company  
PI US 6399578 June 04, 2002  
SO Official Gazette of the United States Patent and Trademark Office Patents,  
(June 4, 2002) Vol. 1259, No. 1, pp. No Pagination.  
<http://www.uspto.gov/web/menu/patdata.html>. e-file.  
ISSN: 0098-1133.  
DT Patent  
LA English  
AB This invention provides conjugates useful for xenotransplantation which  
comprise a galactose alpha1,3 galactosyl (alphaGal) epitope conjugated to  
a \*\*\*valency\*\*\* \*\*\*platform\*\*\* \*\*\*molecule\*\*\*, preferably a  
chemically defined \*\*\*valency\*\*\* \*\*\*platform\*\*\* \*\*\*molecule\*\*\*  
which allows precise valency. The invention also provides compositions  
comprising these conjugates, and methods (such as methods for inducing  
tolerance) using these conjugates and compositions.

L18 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2002 ACS  
AN 2000:881116 CAPLUS  
DN 134:56426  
TI Preparation of molecules containing aminoxy groups as \*\*\*valency\*\*\*  
\*\*\*platform\*\*\* \*\*\*molecules\*\*\* for preparation of bioconjugates.  
IN Jones, David S.; Ton-nu, Huong-thu; Xie, Fang; Tao, Anping; Xu, Tong;  
Hammaker, Jeffrey Robert  
PA La Jolla Pharmaceutical Co., USA  
SO PCT Int. Appl., 113 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
FAN.CNT 1  
PATENT NO. KIND DATE APPLICATION NO. DATE  
PI WO 2000075105 A1 20001214 WO 2000-US15968 20000608  
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR,  
CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU,  
ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU,  
LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD,  
SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU,  
ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,  
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,  
CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG  
EP 1183230 A1 20020306 EP 2000-939762 20000608  
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
IE, SI, LT, LV, FI, RO  
NO 2001006006 A 20020122 NO 2001-6006 20011207  
PRAI US 1999-138260P P 19990608  
WO 2000-US15968 W 20000608  
AB Oxyalkylene mols. contg. .gtoreq.3 aminoxy groups were prepd. Thus,

MeO(CH<sub>2</sub>CH<sub>2</sub>O)<sub>n</sub>CH<sub>2</sub>CH<sub>2</sub>O<sub>2</sub>CN(CH<sub>2</sub>CH<sub>2</sub>OCH<sub>2</sub>CH<sub>2</sub>O<sub>2</sub>CN(CH<sub>2</sub>CH<sub>2</sub>NHCO(CH<sub>2</sub>)<sub>5</sub>NHCO(CH<sub>2</sub>)<sub>5</sub>NH<sub>2</sub>)<sub>2</sub>)  
J2 (n = approx. 503) (prepn. outlined) was stirred with Domain 1  
polypeptide .beta.2GPI-glyoxylic acid reaction product to give the  
tetraadduct, which at 0.17 nmol/rat gave 61% suppression of anti-Domain 1  
antibody in immunized rats.  
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS  
RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 4 OF 6 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS  
INC.  
AN 2002:62199 BIOSIS  
DN PREV200200062199

TI Chemically-defined non-polymeric \*\*\*valency\*\*\* \*\*\*platform\*\*\*  
\*\*\*molecules\*\*\* and conjugates thereof.  
AU Coutts, S. M.; Jones, D. S.; Livingston, D. A.; Yu, L.  
CS Rancho Santa Fe, Calif. USA  
ASSIGNEE: LA JOLLA PHARMACEUTICAL COMPANY  
PI US 5606047 Feb. 25, 1997  
SO Official Gazette of the United States Patent and Trademark Office Patents,  
(Feb. 25, 1997) Vol. 1195, No. 4, pp. 2594-2595.  
ISSN: 0098-1133.  
DT Patent  
LA English

L18 ANSWER 5 OF 6 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS  
INC. DUPLICATE 1  
AN 2002:48444 BIOSIS  
DN PREV200200048444

TI Chemically-defined non-polymeric \*\*\*valency\*\*\* \*\*\*platform\*\*\*  
\*\*\*molecules\*\*\* and conjugates thereof.  
AU Coutts, S. M.; Jones, D. S.; Livingston, D. A.; Yu, L.  
CS Rancho Santa Fe, Calif. USA  
ASSIGNEE: LA JOLLA PHARMACEUTICAL COMPANY  
PI US 5552391 Sept. 3, 1996  
SO Official Gazette of the United States Patent and Trademark Office Patents,  
(Sept. 3, 1996) Vol. 1190, No. 1, pp. 437-438.  
ISSN: 0098-1133.  
DT Patent  
LA English

L18 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2002 ACS  
AN 1995:892826 CAPLUS  
DN 124:290272  
TI Preparation of chemically-defined non-polymeric \*\*\*valency\*\*\*  
\*\*\*platform\*\*\* \*\*\*molecules\*\*\* and conjugates thereof.  
IN Coutts, Stephen; Jones, David S.; Livingston, Douglas Alan; Yu, Lin  
PA La Jolla Pharmaceutical Co., Can.  
SO Eur. Pat. Appl., 78 pp.  
CODEN: EPXXDW  
DT Patent  
LA English  
FAN.CNT 8

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 642798	A2	19950315	EP 1993-309720	19931203
EP 642798	A3	19980916		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
US 6060056	A	20000509	US 1993-118055	19930908
US 5552391	A	19960903	US 1993-152508	19931115
PRAI US 1993-118055	A	19930908		
US 1993-142598	A	19931022		
US 1993-152506	A	19931115		
EP 1993-309288	A	19931122		
US 1990-466138	B2	19900116		
US 1990-494118	A2	19900313		
US 1991-652648	A2	19910208		
US 1992-914869	A2	19920715		

GI

/ Structure 1 in file .gra /

AB Conjugates comprising biol. or chem. mols., including polynucleotide  
duplexes of at least 20 base pairs that have significant binding activity  
for human lupus anti-dsDNA autoantibodies, reacted with valency platforms  
G1(T1)<sub>n</sub>, G2(L2J222(pT2))<sub>m</sub> [G1, G2 = null, (branched) chain contg. 1-2000  
atoms selected from C, N, O, Si, P, S; T1, T2 = NHR, CONHNHR, NHNHR,  
CO<sub>2</sub>H,  
CO<sub>2</sub>R1, CO<sub>2</sub>X, SH, OH, etc.; R = H, alkyl, cycloalkyl, aralkyl; R1 =  
N-succinimidyl, p-nitrophenyl, pentafluorophenyl, etc.; X = halo, other  
leaving group; L2 = null, O, NR, S; J2 = null, CO, CS; Z2 = radical contg.  
1-200 atoms selected from C, H, N, O, Si, P, S, and contg. attachment  
sites for functional groups; n, m = 1-32; p = 1-8; with provisos], were  
prepd. Thus, title conjugate (I; R = H-Trp-Ile-Lys-Arg-Lys-Arg-Gln-Gln-  
Lys-Cys-Gly-OH, bound through a cysteine S atom; n = approx. 74) (prepn.  
given) at 1000 .mu.g/mouse in mice primed and boosted with the parent  
protein melittin gave an 86.8% redn. in peptide specific plaque forming  
cells.

=> d his

(FILE 'HOME' ENTERED AT 14:14:50 ON 26 NOV 2002)

FILE 'BIOSIS, EMBASE, CAPLUS' ENTERED AT 14:30:51 ON 26 NOV 2002  
L1 0 S IMMUNOGENIC VALENCY PLATFORM MOLECULE?  
L2 71 S IMMUNO? (3A) PLATFORM  
L3 1 S L2 AND (SLE OR SYSTEMIC LUPUS ERYTHEMATOSUS)  
L4 3 S L2 AND AFFINITY  
L5 4 S L3 OR L4  
L6 4 DUP REM L5 (0 DUPLICATES REMOVED)  
L7 56 S LJP 394  
L8 40 DUP REM L7 (16 DUPLICATES REMOVED)  
L9 4 S L8 AND AFFINITY?

L10 1 S NON IMMUNOGENIC VALENCY PLATFORM  
 L11 1064 S ANTI-DSDNA ANTIBODY?  
 L12 581 S L11 AND SLE  
 L13 54 S L12 AND AFFINITY?  
 L14 25 DUP REM L13 (29 DUPLICATES REMOVED)  
 L15 25800 S SLE  
 L16 2 S VALENCY PLATFORM MOLECULE  
 L17 7 S VALENCY PLATFORM MOLECULE?  
 L18 6 DUP REM L17 (1 DUPLICATE REMOVED)  
 L19 0 S L18 AND L11

=> s l12 and (oligo? or dsDNA or nucleic acid?)  
 L20 581 L12 AND (OLIGO? OR DSDNA OR NUCLEIC ACID?)

=> s l12 and ((oligo? or dsDNA or nucleic acid?) (3s) conjugat?)  
 L21 11 L12 AND (OLIGO? OR DSDNA OR NUCLEIC ACID?) (3S)  
 CONJUGAT?)

=> dup rem l21  
 PROCESSING COMPLETED FOR L21  
 L22 6 DUP REM L21 (5 DUPLICATES REMOVED)

=> d bib abs 1-y  
 'ACC' IS NOT VALID WITH MULTIFILE PROCESSING

DISPLAY ACC is not allowed in a multifile environment. Enter  
 "DISPLAY HISTORY" to locate the file the L# was created in, use the  
 FILE command to enter that file, and re-enter the DISPLAY ACC  
 command.

=> d bib abs 1-  
 YOU HAVE REQUESTED DATA FROM 6 ANSWERS - CONTINUE? Y(N):y

L22 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2002 ACS  
 AN 2001:129401 CAPLUS  
 DN 134:324842  
 TI A bispecific dsDNA.times.monoclonal antibody construct for clearance of  
 anti-dsDNA IgG in systemic lupus erythematosus  
 AU Lindorfer, M. A.; Schuman, T. A.; Craig, M. L.; Martin, E. N.; Taylor, R.  
 P.  
 CS Department of Biochemistry and Molecular Genetics, University of Virginia  
 Health Sciences Center, Charlottesville, VA, 22908-0733, USA  
 SO Journal of Immunological Methods (2001), 248(1-2), 125-138  
 CODEN: JIMMBG; ISSN: 0022-1759  
 PB Elsevier Science B.V.  
 DT Journal  
 LA English  
 AB High avidity anti-dsDNA IgG antibodies are believed to play an important  
 role in the pathogenesis of the autoimmune disease systemic lupus  
 erythematosus ( "SLE" ) and therefore attempts have been made to  
 reduce the concn. of these antibodies in the bloodstream of "SLE"  
 patients. Previously the authors reported the development of an antigen  
 based heteropolymer (AHP), a bispecific complex prep. by using the  
 avidin-biotin system to crosslink dsDNA to a mAb specific for the human  
 erythrocyte (E) complement receptor. Our studies indicated that this AHP  
 could bind "anti" - "dsDNA" "antibodies" to E and  
 facilitate clearance of these autoantibodies from the circulation of a  
 monkey without E destruction. Here the authors report an improved  
 covalent crosslinking procedure and purifn. scheme in which the AHP  
 construct is isolated by pptn. in 50% satd. ammonium sulfate. The authors  
 used a dsDNA binding dye, PicoGreen, to demonstrate specificity of binding  
 of dsDNA to E via the AHP. The efficacy of the AHP in binding IgG  
 "anti" - "dsDNA" "antibodies" to E was demonstrated in  
 a sensitive and quant. assay, based on the time resolved fluorescence  
 properties of europium-labeled anti-human IgG mAbs used to probe the E.  
 the authors also used this assay to screen "SLE" patient and  
 normal plasmas for levels of anti-dsDNA IgG. The results of this assay  
 correlate very well with the Farr assay, and therefore this approach may  
 be useful in the development of informative and specific assays for a  
 variety of autoantibodies. Treatment of "SLE" plasmas with E-AHP  
 under conditions close to physiol. led to substantial redns. (gtoreq.  
 90%) in anti-dsDNA titers. It should be possible to test these new AHP  
 for their ability to target and safely remove IgG "anti" -  
 "dsDNA" "antibodies" from the circulation in animal models.  
 RE.CNT 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2002 ACS  
 AN 2000:325877 CAPLUS  
 DN 133:72848  
 TI Use of anion exchange resin-packed capillary column for rapid detection of  
 anti-double-stranded DNA antibody in systemic lupus erythematosus serum  
 AU Lim, Tae-Kyu; Nakamura, Noriyuki; Matsunaga, Tadashi  
 CS Department of Biotechnology, Tokyo University of Agriculture and  
 Technology, Tokyo, 184-8588, Japan  
 SO Biotechnology and Bioengineering (2000), 68(5), 571-575  
 CODEN: BIBIAU; ISSN: 0008-3592  
 PB John Wiley & Sons, Inc.  
 DT Journal  
 LA English  
 AB An anti-double-stranded (ds) DNA antibodies in serum-detection system was  
 developed based on flow immunoassay with packed-capillary column. Alk.

phosphatase "conjugated" DNA (ALP-DNA) and "anti" -  
 "dsDNA" "antibody" were sepd. from unreacted ALP-DNA on the  
 basis of the difference in isoelec. point. A linear "anti" -  
 "dsDNA" "antibody" dose-response curve was obtained between  
 luminescence intensity and concn. of "anti" - "dsDNA"  
 "antibody" in the range 25-200 IU/mL. This simple technique permits  
 the assay of anti- "dsDNA" autoimmune antibodies within 7 min.  
 These results give reduced detection times compared with those previously  
 reported through the use of capillary columns.

RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 3 OF 6 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS  
 INC.DUPLICATE 1  
 AN 1997:66348 BIOSIS  
 DN PREV199799365551  
 TI Anti-double stranded DNA antibodies in systemic lupus erythematosus:  
 Detection and clinical relevance of IgM-class antibodies.  
 AU Bootsma, H. (1); Spronk, P. E.; Hummel, E. J.; De Boer, G.; Ter Borg, E.  
 J.; Limburg, P. C.; Kallenberg, C. G. M.  
 CS (1) Dep. Internal Med., Division Rheumatol., Univ. Hosp. Groningen, P.O.  
 Box 30.001, NL-9700 RB Groningen Netherlands  
 SO Scandinavian Journal of Rheumatology, (1996) Vol. 25, No. 6, pp. 352-359.  
 ISSN: 0300-9742.  
 DT Article  
 LA English  
 AB We determined the discriminative value of the Farr assay in comparison to  
 ELISA and Crithidia luciliae immunofluorescence assay (IFT) for detecting  
 "anti" - "dsDNA" "antibodies" as a diagnostic tool for  
 systemic lupus erythematosus ( "SLE" ). Special attention was paid to  
 the diagnostic significance of IgM-class anti- "dsDNA" . Sera  
 were analyzed from 74 patients with "SLE" , 257 patients with other  
 auto-immune diseases, and 50 healthy controls. All sera were tested for  
 anti- "dsDNA" using the IFT (anti-total immunoglobulin  
 "conjugate" ), ELISA (anti-IgG and anti-IgM "conjugates" ),  
 and the 125I Farr assay. Specificity and sensitivity for a diagnosis of  
 "SLE" appeared to be highest for the Farr. All "SLE" sera  
 with IgM-class anti- "dsDNA" without IgG-class anti- "dsDNA"  
 as detected by ELISA, were positive when tested by the Farr assay. In  
 contrast, most of the sera with IgM-class anti- "dsDNA" as detected  
 by ELISA from patients with diseases other than "SLE" were  
 negative when tested by Farr assay.

L22 ANSWER 4 OF 6 EMBASE COPYRIGHT 2002 ELSEVIER SCI.  
 B.V.DUPLICATE 2  
 AN 94243111 EMBASE  
 DN 1994243111  
 TI "Conjugates" or "dsDNA" linked to human gammaglobulin  
 inhibit "anti" - "dsDNA" "antibodies" in vitro  
 AU Mikael N.; Boguniewicz M.; Manakata Y.; Sasaki T.; Borel H.; Borel Y.  
 CS Nat Jewish Ctr for Imm and Resp Med, 1400 Jackson Street, Denver CO  
 80206,  
 United States  
 SO Lupus, (1994) 3/3 (173-179).  
 ISSN: 0961-2033 CODEN: LUPUES  
 CY United Kingdom  
 DT Journal; Article  
 FS 026 Immunology, Serology and Transplantation  
 031 Arthritis and Rheumatism  
 LA English  
 SL English  
 AB Previous studies have shown that both nucleosides and  
 "oligonucleotides" linked to isologous gammaglobulin suppress anti-  
 "nucleic" "acid" antibody production both in vivo and in  
 vitro. The aim of this study was to determine whether one can make a  
 DNA-human gammaglobulin (HGG) "conjugate" which can inhibit  
 anti-double stranded DNA ( "dsDNA" ) antibodies obtained from a  
 heterogeneous population of systemic lupus erythematosus ( "SLE" )  
 sera. To do so, we constructed "conjugates" of sonicated  
 "dsDNA" fragments of 100-400 base pairs covalently linked to HGG  
 with varying degrees of substitution of DNA:HGG. An ELISA inhibition assay  
 was used to determine which "conjugate" best inhibits the binding  
 of "anti" - "dsDNA" "antibodies" . "Conjugate"  
 2, prepared with monomelic HGG (150kD) with a high degree of substitution  
 (3.72 DNA:HGG) inhibited the binding of "anti" - "dsDNA"  
 "antibodies" from 27 of 31 "SLE" sera. In addition, this  
 "conjugate" inhibited the spontaneous formation of anti-  
 "dsDNA" in vitro by cultured lymphoid cells from selected  
 "SLE" patients. Together, this data suggests that a 'generic'  
 tolerogen may provide an antigen specific therapy for "SLE" .

L22 ANSWER 5 OF 6 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS  
 INC.DUPLICATE 3  
 AN 1989:182029 BIOSIS  
 DN BA87:93295  
 TI IN-VITRO MANIPULATION OF HUMAN ANTI-DNA ANTIBODY PRODUCTION  
 BY  
 ANTI-IDIOTYPIC ANTIBODIES CONJUGATED WITH NEOCARZINOSTATIN.  
 AU SASAKI T.; TAMATE E.; MURYO I.; TAKAI O.; YOSHINAGA K  
 CS SECOND DEP. INTERN. MED., TOHOKU UNIV. SCH. MED., SEIRYOCHO  
 1-1, SENDAI  
 980, JPN.

SO J IMMUNOL, (1989) 142 (4), 1159-1165.

CODEN: JOIMA3. ISSN: 0022-1767.

FS BA; OLD

LA English

AB Anti-DNA Id, 0-81, consist of 5 to 51% of Id in human anti-ssDNA antibodies; NE-1-Id shares 2 to 20% of those in \*\*\*anti\*\*\*. \*\*\*dsDNA\*\*\*. \*\*\*antibodies\*\*\*. Thus, both 0-81-Id and NE-1-Id are of the cross-reactive Id that are commonly present among anti-DNA antibodies. In order to manipulate the production of anti-DNA antibodies by human PBL, we used mouse anti-idiotypic mAb or those \*\*\*conjugated\*\*\* with acytotoxic agent, neocarzinostatin. Treatment with the \*\*\*conjugates\*\*\* caused profound suppression of anti-ssDNA and \*\*\*anti\*\*\*. \*\*\*dsDNA\*\*\*. \*\*\*antibody\*\*\* synthesis related to 0-81 and NE-1-Id. This was attributed to the specific killing of the clones bearing anti-DNA Id among the lymphocytes, evidenced by the indirect rosette formation tests. The Id-mediated suppression was not solely due to selective elimination of Id-positive B cells, because 50 to 92% of anti-DNA antibodies were suppressed by treatment with the \*\*\*conjugates\*\*\*. This was supported by flow cytometry analysis that showed a decrease of anti-Id-reactive cells when T cells were treated with the \*\*\*conjugates\*\*\*. This method, then, will permit an analysis of the question as to whether T cells reactive to anti-idiotypic antibodies might participate in the regulatory mechanism for anti-DNA production and, in addition, may lead to a new therapy for \*\*\*SLE\*\*\*.

L22 ANSWER 6 OF 6 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 4

AN 1978:239940 BIOSIS

DN BA66:52437

TI ANTIBODIES TO DOUBLE STRANDED DNA A COMPARISON OF THE INDIRECT IMMUNO FLUORESCENT TEST USING CRITHIDIA-LUCILIAE AND THE DNA BINDING ASSAY.

AU DEEGAN M J; WALKER S E; LOVELL S E

CS DEP. PATHOL., UNIV. MICH., ANN ARBOR, MICH. 48109, USA.

SO AM J CLIN PATHOL, (1978) 69 (6), 599-604.

CODEN: AJCPAI. ISSN: 0002-9173.

FS BA; OLD

LA English

AB A new indirect immunofluorescent test for detecting anti-double-stranded DNA ( \*\*\*dsDNA\*\*\* ) antibodies was evaluated and the results compared with those of the DNA-binding test (modified Farr assay). The substrate, C. luciliae (CL), is a nonpathogenic trypanosome containing a kinetoplast of \*\*\*dsDNA\*\*\*. The test was performed with fluorescein-\*\*\*conjugated\*\*\* polyvalent (anti-Ig[immunoglobulin]G, -IgA and -IgM) and monospecific anti-Ig antisera. Sera from 57 patients (75 specimens) with systemic lupus erythematosus ( \*\*\*SLE\*\*\* ), 30 patients with rheumatoid arthritis, 31 patients with scleroderma, 59 patients with other rheumatic diseases and 31 normal individuals were studied. Thirty-three of the 51 \*\*\*SLE\*\*\* sera with positive DNA-binding tests (binding > 20%) also had positive CL tests. The 18 CL-negative, DNA-binding-positive sera had DNA-binding values between 20 and 45%. Anti- \*\*\*dsDNA\*\*\* were usually IgG, often accompanied by IgM and occasionally IgA antibodies. Sera of 8 patients who had conditions other than \*\*\*SLE\*\*\* were CL-positive, DNA-binding-negative. The CL test is a simple and reproducible method for detecting \*\*\*anti\*\*\*. \*\*\*dsDNA\*\*\*. \*\*\*antibodies\*\*\*, but in its present form is not as sensitive as the DNA-binding test.

=> s ds on (3a) conjugat?

L23 51 DS ON (3A) CONJUGAT?

=> s l23 and (non immunogen? carrier or nonimmunogenic carrier)

L24 0 L23 AND (NON IMMUNOGEN? CARRIER OR NONIMMUNOGENIC CARRIER)

=>

Connection closed by remote host

---Logging off of STN---

END

Unable to generate the STN prompt.  
Exiting the script...